Introduction

Various interventional procedures are performed for the diagnosis of portal hypertension (PH) and treatment of its complications. Hepatic venous pressure gradient (HVPG) is useful in diagnosis of PH before the clinical signs appear. Other uses of HVPG are diagnosis of the type of PH, measuring response to therapy, and prediction of morbidity and mortality. Similarly in patients with deranged coagulation and ascites, transjugular liver biopsy (TJLB) is done to diagnose the cause of liver parenchymal disease in patients with deranged coagulation or having ascites. Transjugular intrahepatic portosystemic shunt (TIPS) and balloon retrograde transvenous obliteration (BRTO) are used for the treatment of various complications of PH. TIPS has an important role in the treatment of variceal bleeding, refractory ascites, hepatic hydrothorax, hepatorenal syndrome (HRS), and Budd–Chiari syndrome (BCS), whereas BRTO is used in gastric variceal bleeding and hepatic encephalopathy (HE). This article attempts to provide evidence-based guidelines on the management of portal hypertension and treatment of its complications.
Guidelines on the management of PH and treatment of its complications.

Methods

According to the mandate of the Indian College of Radiology and Imaging, the guidelines were formulated. The guidelines were formed based on the available literature in this subspecialty by interventional radiologists working exclusively in the management of PH. The authors performed extensive literature search of PubMed, Cochrane library, and Embase database and framed the guidelines in the form of statements, and the grades of recommendation were assigned (1 = strong, 2 = weak) and quality of evidence (A = high, B = moderate, C = low) as defined by UpToDate grading guide [https://www.uptodate.com/home/grading-guide].

The statements and the discussion have stressed upon the clinical features, indications, contraindications, techniques, and complications of various procedures in the management of PH as may be important for an interventional radiologist focusing on PH.

1.1 Clinical presentation of patients with PH

The patients present with variceal bleed, ascites, and HE. (1A)

1.2 Investigations required for the diagnosis of PH

Laboratory investigations: Baseline investigations required are liver function tests, kidney function tests, platelet count, international normalized ratio (INR), and serum albumin levels. (1A)

Ultrason (US) and cross-sectional imaging including multiphasic contrast-enhanced CT and MRI: Imaging is important in diagnosing chronic liver disease and its complications. (1A).

Non-invasive methods of measuring portal hypertension: Serum biomarkers like AST–platelet ratio index, fibroindex (combination of platelet count, AST, and GGT), and FIB4 (combination of age, AST, platelet count, and ALT) can be used

Transient elastography: Transient elastography (TE) is used to measure the stiffness of the liver and assess the degree of fibrosis non-invasively. (1A)

1.3 Interventionsal procedures in diagnosing PH

1.3.1 Hepatic venous pressure gradient measurement

HVPG measurement is essential for patients with liver parenchymal disease suspected to have PH. (1A)

Indications: Indications of HVPG measurement are diagnosis of degree of PH (1A), prognostic information (1A), measurement of response to therapy (1A), predictor of response to antiviral therapy (1A), assessment of development for hepatocellular carcinoma (HCC) (2B), and trials for investigations of new therapies. (2C)

Contraindications: There are no absolute contraindications for HVPG measurement. The relative contraindications for HVPG measurements are severe cardiac or pulmonary disease, hypersensitivity to contrast agents, pregnancy. (1A)

Pre-procedural evaluation: Review indications and contraindications, informed consent to be taken, patient should be fasting for 6 hours, check coagulation parameters. (1A)

The pressure recorder should be calibrated (1C)

Procedure of measuring HVPG: (a) Venous puncture should be done under US guidance; (b) right atrium (RA) and IVC pressures should be measured; (c) right hepatic vein accessed and pressure should be measured within 5 cm of the ostium; (d) after the wedge hepatic venous pressure (WHVP) is taken, contrast is injected to assess adequate occlusion; (e) three permanent readings are taken, and mean is calculated. (1A)

Complications: complications include hematoma at the puncture site, transient arrhythmias, AV fistula formation, pneumothorax, and hemothorax. (1A)

1.3.2 Transjugular liver biopsy

Pre-procedural evaluation: (a) Coagulation parameters (INR and platelets) should be evaluated. (b) Patient should be fasting for 4 to 6 hours. (c) An US screening to assess the patency of IJV and hepatic veins should be done. (1A)

Right IJV approach should be used (1B) alternatively; femoral approach may also be used.

Indications: Indications of TJLB are ascites, coagulopathy, morbid obesity, shrunken liver, peliosis hepatis, hereditary hemorrhagic telangiectasia, and early post living donor liver transplant (LDLT) graft dysfunction. (1C)

Contraindications: Relative contraindications are right IJV thrombosis, hepatic vein thrombosis, and hydatid cyst of the liver. (1A)

Three cores should be obtained to ensure adequate tissue sampling. (1B)

Pre- and post-procedural contrast run should be taken. (1A)

Complications: Hemoperitoneum is a major complication of TJLB. Minor complications like biliary puncture, portal vein puncture, transient arrhythmias, and puncture site hematomas. (1A)

1.4 Management of complications of PH

1.4.1 Management of uncomplicated ascites

Patients present with increasing abdominal distension. (1A)

Diagnostic paracentesis is to be done in patients with grade II and grade III ascites. (1A)

Grade II ascites is treated with diuretics (1A) and salt restriction. (1A)

Grade III ascites is treated with large-volume paracentesis (LVP). (1A)

Refractory ascites is treated by repeated LVP (1A) or TIPS. (1A)

Tunneled catheters may be used for refractory ascites. (2B)

Peritoneovenous shunting may be done in patients who are poor candidates for repeated paracentesis, TIPS, or liver transplant. (2B)

1.4.2 Management of variceal bleeding

1.4.2.1 Management of esophageal variceal bleeding
Pharmacotherapy and endoscopic therapy is the first line of treatment in acute esophageal varical bleeding. (1A) TIPS is used in the treatment of acute esophageal varical bleeding after failure of medical and endoscopic therapy, pre-emptive TIPS in high-risk patients and secondary prophylaxis. (1A)

1.4.2.2 Management of gastric varical bleeding

Pharmacotherapy and endoscopic therapy are the first line of treatments in acute gastric varical bleeding. (1A) TIPS is used in the treatment of gastroesophageal varical types 2 (GOV2) and isolated gastric varices (IGVs) type 1. (1B)

BRTO is effective in treating gastric varices. (1C)

BRTO may be advantageous over TIPS in the treatment of gastric varices. (2A)

1.4.3 HE

BRTO is useful in the treatment of HE. (2A)

1.4.4 Hepatic hydrothorax

Hepatic hydrothorax presents with recurrent pleural effusion. (1A)

Pharmacotherapy is used as a first-line therapy for treatment. (2B)

Refractory hydrothorax may be treated by (a) therapeutic aspiration (1C), (b) pleural catheters (1C), (c) Pneurodesis (1B) and (d) TIPS (1B)

1.4.5 Treatment of HRS

HRS is treated with Terlipressin and albumin. (1A)

TIPS may be used in HRS (type 2). (2A)

1.4.6 Budd–Chiari syndrome

Clinical presentation of BCS is variable. (1A)

USG with Doppler should be used as first modality for the diagnosis of BCS, followed by CT/MRI. (1A)

Anticoagulants are the first line of treatment for asymptomatic BCS. (1A)

Venoplasty with/without stenting is used for short segment IVC or hepatic vein stenosis. (1A)

TIPS/Direct intrahepatic portosystemic shunt (DIPS) is done in patients who do not respond to anticoagulation and/or venoplasty/stenting is not possible. (1A)

2.0 Interventional procedures and techniques for the treatment of PH

2.1 Transjugular intrajugular portosystemic shunt (TIPS)

Indications of TIPS: Indications are acute varical bleeding (1A), refractory ascites (1A), refractory hydrothorax (1B), portal vein thrombosis (PVT) (1C), HRS (2B), and BCS (1A)

Absolute contraindications of TIPS: Contraindications are congestive cardiac failure, severe tricuspid regurgitation, severe pulmonary hypertension (mean pulmonary artery pressure >55 mm Hg), sepsis, and biliary obstruction. (1A)

Relative contraindications of TIPS: Severe coagulopathy, severe thrombocytopenia, encephalopathy, moderate pulmonary hypertension (mean pulmonary artery pressure 41–55 mm Hg), centrally located liver mass (1A)

TIPS should be performed by an experienced interventional radiologist in a tertiary care center. (1A)

Prior to TIPS liver function tests, renal function tests, coagulation profile, Child–Pugh (CP) score, MELD score and echocardiography should be done. (1A)

US with Doppler, contrast-enhanced CT and/or MRI should be done prior to the procedure. (1A)

Preferred route for TIPS is right internal jugular vein and USG-guided IJV puncture should be done. (1A)

Right hepatic vein is preferred for the creation of TIPS. (1A)

USG-guided portal vein puncture is preferable. (1B)

Covered stents should be preferred over bare stents for TIPS. (1A)

Goal of TIPS is to reduce portosystemic gradient to <12 mm Hg. (1A)

In patients with varical bleed, if portosystemic gradient is not reduced below 12 mm Hg, additional embolization of varices arising from splenoportal axis may be done. (2B)

TIPS in PVT is feasible and also may aid in the resolution of thrombus. (1C)

Complications of TIPS: (a) HE, (b) puncture-related complications including hemoperitoneum, (c) stent-related complications, (d) hepatic dysfunction. (1B)

2.2. BRTO

Indications: Gastric varical bleeding and HE. (1A)

Contraindications: Severe coagulopathy, splenic vein thrombosis, PVT, and intractable esophageal varical bleed. (1B)

Pre-procedural imaging evaluation (multiphasic CT is necessary). (1B)

Femoral or jugular route may be taken as per the anatomy of renal vein/ lienorenal shunt. (1B)

Sodium tetradecyl sulfate is easily available, safe, and effective sclerosant for BRTO. (1B)

Compliant balloon catheter should be used for occluding the shunt and the shunt should be occluded for at least 4 to 6 hours. (1B)

End point of sclerosant administration is filling of the entire varix. (1B)

Modifications of BRTO with the use of vascular plug (plug-assisted retrograde transvenous obliteration, PARTO) is a faster technique and does not require sclerosant nor is associated with complications like balloon rupture/ballon displacement. (1B)

Complications of BRTO/PARTO: Exacerberation of ascites/pleural effusion, exacerbation of esophageal varices, portal venous thrombosis, gastropathy. (1A)

Detailed Guidelines

PART 1

1. Clinical presentation

Q1. What is the clinical presentation of PH?

The common complications of PH are varical bleeding, ascites, and HE.
Remarks

PH is the result of increasing vascular resistance due to parenchymal distortion and increased portal venous flow due to hyperdynamic circulation.\textsuperscript{1,2} PH is diagnosed when HVPG is >5 mm Hg. The complications of PH develop when the HVPG is >10 mm Hg. Gastrointestinal manifestations of PH are formation of gastroesophageal varices (GOV), ectopic varices, intestinal vasculopathy, ascites, and spontaneous bacterial peritonitis. Neurological manifestation of PH is HE. Pulmonary manifestations of PH are hepato-pulmonary syndrome, porto-pulmonary hypertension, and hepatic hydrothorax. Renal involvement results in HRS. Other manifestations are cardiomyopathy, hepatic osteodystrophy, and hypersplenism.\textsuperscript{3,4}

Q2. What laboratory investigations are required to evaluate a patient with PH?

Baseline investigations required are liver function tests, kidney function tests, platelet count, INR, and serum albumin levels.

Remarks

The baseline investigations are an insight to the functional status of the liver. Calculation of CP score which uses bilirubin, INR, ascites, albumin, and encephalopathy is used to assess the severity of the liver disease. Increasing CP score is associated with decreasing mean survival.\textsuperscript{5} The model for end-stage liver disease (MELD) score uses bilirubin, INR, and creatinine levels and is used for risk of mortality in patients with cirrhosis. Patients with higher MELD scores are more likely to present with variceal re-bleed. INR and platelet levels are important if an interventional procedure is being planned to determine the risk of bleeding.\textsuperscript{5,6}

Q3. What is the role of imaging in PH?

Imaging is important in diagnosing chronic liver disease and its complications.

Remarks

US is cheap, non-invasive, and widely available. Grayscale US assesses the parenchymal echo texture, measures the portal vein diameter, and detects the presence of large collaterals. Other findings like splenomegaly and ascites can also be detected. Doppler US assesses the direction of flow in the portal vein in addition to various parameters like velocity, resistive index and pulsatility index of the portal vein.\textsuperscript{7,8} Multiphasic CT is needed to assess the hepatic parenchyma, presence of space-occupying lesion, status of hepatic veins, inferior vena cava, portal vein, and portosystemic collaterals. Due to its ability of comprehensively depicting the portosystemic collaterals, multiphasic CT is useful for pre-procedural evaluation in BRTO and its follow-up.\textsuperscript{9–11} MRI similar to CT depicts the anatomy of the liver and the hepatic vasculature, presence or absence mass lesion, vascular thrombosis and presence of large collaterals. Recently, MR elastography (MRE) has also been used for the measurement of liver stiffness. MRE has few added advantages over US elastography. It can evaluate the entire liver and can be done in obesity or ascites, which is a limitation of US elastography. Longer scanning times, availability, and higher cost are the disadvantages of MRL. MRE has been used in measuring the stiffness of the liver and the spleen with promising results.\textsuperscript{12,13} Various imaging modalities do not directly measure the portal pressure and do not correlate well with HVPG.

Q4. Are there non-invasive methods of measuring PH?

Remarks

Serum biomarkers and TE have been used to predict PH. TE has been compared with various serum biomarkers like AST-platelet ratio index, fibroindex (combination of platelet count, AST and GGT), and FIB4 (combination of age, aspartate transaminase, platelet count, alanine aminotransferase) and was found to be more sensitive, specific, and accurate. Serum biomarkers correlate well with liver fibrosis while the detection of PH is suboptimal.\textsuperscript{14,15}

Q5. Does TE have a role in PH?

TE is used to measure the stiffness of the liver and assess the degree of fibrosis.

Remarks

TE is a widely available non-invasive modality that has been used to measure the degree of fibrosis in chronic liver disease.\textsuperscript{14} Recently Baveno VI consensus workshop recognized a subset of asymptomatic patients with advanced cirrhosis having HVPG >5 mm Hg. These patients were labeled as compensated advanced liver disease (cALD) or compensated cirrhosis (CC). TE was recommended in these patients as it has been useful in early detection of liver fibrosis and progression to clinically significant PH (CSPH) which is defined as HVPG >10 mm Hg. CSPH patients are at an increased risk of developing complications of PH. In the absence of other clinical signs, TE values <10 kPa rule out cALD or CC. Values >15 kPa are suggestive of CC. It was also ascertained that screening endoscopy can be avoided in patients with liver stiffness <20 kPa and platelet count >150,000 as these patients have very lower risk of vari-\textsuperscript{16} es. Since the elastography findings can be variable, TE has to be performed twice on two different days. Obesity and ascites are detrimental to measurement of TE and falsely high for conditions in which liver is congested like right heart failure, extrahepatic cholestasis, and alcoholism.\textsuperscript{17,18}

Q6. What is the role of measuring HVPG in chronic liver disease?

HVPG measurement is essential for patients with chronic liver disease.

Remarks

HVPG is the gold standard for the measurement of portal venous pressure in chronic liver disease. Normal HVPG is <5 mm Hg. HVPG >5 mm Hg is labeled as mild PH and this phase does not have any clinical manifestations. HVPG >10 mm Hg is labeled CSPH and is associated with the development of complications like ascites and variceal bleeding and increasing mortality. HVPG identifies and classifies PH.\textsuperscript{19}
Q7. What are the indications for the measurement of HVPG?
- Diagnosis of the degree of PH.
- Prognostic information.
- Measurement of response to therapy.
- Assessment of the risk of developing HCC.
- Predictor of response to antiviral therapy.
- Clinical trials for investigation of new therapies.

Remarks

HVPG diagnoses PH and predicts the outcome of patients depending on the values. HVPG >10 mm Hg is associated with onset of complications of PH. Patients with HVPG >12 mm Hg are more likely to be associated with ascites and variceal bleeding.19,20 HVPG values ≥16 mm Hg are associated with increased mortality in the presence or absence of varices that may or may not have bled. At these HVPG values, a patient presenting with variceal bleeding is more likely to have a prolonged hospital stay, increased requirements of blood products, increased chances of early re-bleed and failure to control bleeding. HVPG was also found to be an independent predictor of development of HCC.21,22 Monitoring of HVPG as a response to therapy is also beneficial.23 Since response to pharmacological agents is measurable, HVPG has been used for measuring the response to various pharmacological agents.20,24–29

Q8. What are the contraindications for HVPG measurement?
- Severe cardiac or pulmonary disease.
- Hypersensitivity to contrast agents.
- Pregnancy.
- Active encephalopathy.

Remarks

Cannulation of the right side of the heart can potentially raise right heart pressure and induce or exacerbate cardiac failure. A history of hypersensitivity to contrast agents should be taken as necessary precautions can be followed, though the amount of contrast injected is very low. Patient with active encephalopathy will not be able to lie still and hence variations in HVPG may occur.30,31

Q9. What are the pre-procedural requirements?

Remarks

Review of the indications and contraindications should be done to reduce the incidence of complications. If a concomitant TJLB is also required, right jugular puncture has to be done.30

Q9a. How long the patient should be fasting?

Patient should be fasting for 4 to 6 hours prior to the procedure.

Remarks

The patient should be fasting 4 to 6 hours prior to the procedure as light sedation might be needed for the procedure. American Society of Anaesthesiologists recommends that patient should not have had clear liquids 2 hours prior to the procedure and a light meal 6 hours prior to the procedure. This is to prevent any chance of aspiration during the procedure under sedation.31

Q9b. Is coagulation correction required?

HVPG is a low-risk procedure. Society of Intervention Radiology consensus guidelines state that procedures with low bleeding risk require a minimum platelet count of \(20 \times 10^9/L\) and corrected INR between 2.0 and 3.0.22,32,33

Q10. How is the pressure recorder calibrated?

Remarks

A scale with upper limit of 30 to 60 mm is used with a recording speed of 4 to 5 mm/s. Known external pressure should be used to calibrate the transducer. The transducer should be at the level of the RA and in the mid-axillary line. The tubing should be as short as possible with no air bubbles or leakages.27,28,33

Q11. HVPG measurement

Q11 a. Why should the puncture be US guided?

Remarks

US-guided puncture reduced inadvertent puncture of the artery and hence reduced the chances of post-procedural hematoma or arteriovenous fistula. The various approaches are femoral vein, internal jugular vein (IJV), and the antecubital vein. Right IJV is preferred if a concomitant biopsy is also planned.27,28,33

Q11b. Why should RA and IVC pressures be measured?

Remarks

Using RA pressures will give the true portosystemic gradient and is more relevant if there is stenosis or webs in the hepatic vein or the IVC. IVC pressure should be measured at the level of hepatic ostia. Any pressure below this level may be higher due to compression of the vein by enlarged caudate lobe.27,28,33

Q11c. Where should the pressure be measured in the hepatic vein?

Remarks

The pressure should be measured within 5 cm of the ostium as the readings may be false distally. The difference in free hepatic venous pressure (FHV) and inferior vena cava/right atrium is less than 2 mm Hg. If the pressure is >2 mm Hg, an incomplete occlusion of the vein by the balloon or hepatic vein obstruction should be suspected.27,28,33

Q11d. When should adequate wedging be checked?

Remarks

The adequacy of wedging should be checked after the WHVP is measured. Measurement of WHVP after contrast injection is likely to reveal false values as contrast transmits pressure poorly. In addition, the pressure tracing should be
allowed to stabilize for at least 60 seconds and 15 seconds for measuring WHVP and FHVP, respectively. Adequate wedging can be confirmed by no aspiration of blood on applying negative pressure and by wedge sinusoidogram with no reflux of contrast into other veins and lack of a waveform. If the occlusion is inadequate, the WHVP is measured again and occlusion is reassessed.\textsuperscript{27,28,33}

Q11e. How many readings should be taken?
Remarks
Three permanent readings are taken. If any reading varies by >1 mm Hg, then all the readings are discarded and fresh readings taken as any variation is likely due to an error during recording. Any movement, coughing, or talking by the patient has to be recorded and this might affect the readings.\textsuperscript{27,28,33}

Q12. What are the complications of HVPG and how to avoid them?
Remarks
Puncture site hematomas are the most common complication and can be dealt with post-procedural compression for 10 minutes. Arteriovenous fistula formation can be avoided by using US guidance for puncture. Right hemothorax or pneumothorax can be avoided by not making a low-neck puncture and transgressing the pleura. Transient arrhythmias can be seen when the wire or the catheter traverses the RA.\textsuperscript{27,28,33}

Q13. What are the pre-procedural requirements for TJLB?
Remarks
According to the Society of Intervention Radiology Guidelines, TJLB is a low bleeding risk procedure and recommend that INR be corrected in the range of 2.0 to 3.0 and platelet count >20 x 10$^9$/L.\textsuperscript{32,33} Wallace et al studied the hemorrhagic complications in patients with hematologic malignancies with thrombocytopenia and found that no hemorrhage-related complications occurred. They concluded that the safe platelet count for a TJLB lies below 30 x 10$^9$/L.\textsuperscript{34,35} If the INR is not in the desired range, fresh frozen plasma can be transfused and similarly platelet infusion can also be given for desired platelet levels. There is approximately 6,000/mL increase in platelet after transfusion of a unit of random donor platelets and 30,000/mL increase after transfusion of a unit of single donor platelets.\textsuperscript{34}

Q13b. How long should the patient be fasting for TJLB?
Remarks
Patient should be fasting for at least 2 hours for liquids and 6 hours for light food as per American Society of Anaesthesiology recommendations.\textsuperscript{31}

Q13c. Why should an US screening be done prior to TJLB?
Remarks
IJV should be screened to rule out thrombosis which if present will result in inability to perform TJLB. Similarly in case of thrombosis of hepatic veins, TJLB would not be feasible.\textsuperscript{36}

Q14a. What is the best approach for TJLB?
Remarks
Right IJV is the best approach for TJLB under US guidance. US guidance reduced the chances of complications like carotid puncture, pneumothorax, or hemothorax in addition to assessing the patency of the right IJV.\textsuperscript{36–38}

Q14b. Are there alternative routes for TJLB if right IJV is thrombosed?
Remarks
Transfemoral–transcaval biopsies have been performed by few authors with no significant complications. Cynamon et al performed transfemoral–transcaval biopsy with a technical success of 97%.\textsuperscript{39} Li et al performed liver biopsy via the transfemoral route in LDLT patients reporting a technical success in all patients with adequate biopsy sample and no major complications.\textsuperscript{40} Yavuz et al performed TJLB via left IJV in patients in whom right IJV could not be cannulated.\textsuperscript{41} They reported chest pain in few patients when the stiff cannula passed through the mediastinal veins. No major complications were reported. Right external jugular vein (EJV) approach was used by Siegel et al.\textsuperscript{42} Due to superficial course of the EJV, they recommended the use of this route for other transjugular procedures too.

Biopsies using the abovementioned non-conventional routes should be performed by experienced interventional radiologists and chances of complications are high.

Q15. What are the indications for TJLB?
Remarks
- Ascites
- Coagulopathy
- Morbid obesity
- Small shrunken liver
- Suspected vascular mass or peliosis hepatis
- Hereditary hemorrhagic telangiectasia
- Early postoperative live DLT graft dysfunction

Q16. What are the contraindications for TJLB?
The relative contraindications for TJLB are:
- Right IJV thrombosis.
- Hepatic veins thrombosis.
- Hydatid cyst of the liver.
Right IJV and hepatic vein thrombosis limit the access to the liver and hence the biopsy cannot be done via this route. Inadvertent puncture of the hydatid cyst may result in hematogenous dissemination and severe life-threatening anaphylaxis.  

Q17. How many cores should be obtained?

Three cores should be obtained.

Remarks

The biopsy specimen should have at least 11 portal tracts or should be at least 20 to 25-mm long for appropriate histopathological diagnosis. Short specimens may result in failure to diagnose cirrhosis in 20% cases.  

Q18. Why pre- and post-procedural contrast runs important?

Remarks

After cannulation of the right hepatic vein, a contrast injection is done to verify the position as a distal position can result in hepatic capsule puncture and resultant hemoperitoneum. A contrast injection post-biopsy can identify the peritoneal leakage of contrast and if visualized embolization of the vein can be done immediately.  

Q19. What are the complications of TJLB?

Remarks

Hemoperitoneum is a major complication of TJLB. A contrast injection into the hepatic vein just after biopsy can diagnose peritoneal leakage of contrast and an immediate embolization with gelfoam can be done. If there is a fall in hemoglobin, multiphasic CT should be done and if the bleed is arterial, selective angiography and embolization should be done.

Minor complications are self-limiting. Puncture site hematomas can be treated by manual compression.  

Q20. How do patients with uncomplicated ascites present?

Remarks

Non-infected ascites and ascites not associated with HRS are called uncomplicated ascites. There are three grades of ascites; grade I which can be detected only by US, grade II which shows symmetric distension of the abdomen, and grade III which shows marked abdominal distension. Onset of ascites in PH is a poor prognostic indicator.  

Q21. When should a diagnostic paracentesis be done?

Remarks

A diagnostic paracentesis should be done in all patients who develop grade II and grade III ascites to rule out other causes of ascites. An ascites with serum ascites albumin gradient ≥1.1 g/dL is likely to due to PH. Total ascitic protein level should be measured as levels <15 g/L are associated with increased chances of spontaneous bacterial peritonitis. In addition, neutrophil count and cultures should also be sent.  

Q22. How is grade II ascites treated?

Remarks

Grade II ascites is treated by diuretics and salt restriction.  

Patients developing moderate ascites are started on aldosterone antagonists with sequential increase in dose till it reaches the maximum. If the weight loss is <2 kg/wk or hyperkalemia occurs, then furosemide is added in increasing doses. A moderate sodium restriction is suggested.  

Q23. How is grade III ascites treated?

Remarks

Grade III ascites is treated with LVP.  

LVP should be done with simultaneous administration of albumin, especially if >5 L fluid is to be drained. Concomitant administration of albumin reduces the incidence of post-paracentesis circulatory dysfunction which has detrimental effects like early re-accumulation, increasing portal pressure, and development of HRS. Minimal dose of diuretics should be started after LVP.  

Q24. How is refractory ascites treated?

Remarks

Refractory ascites is defined as ascites which cannot be mobilized or early recurrence which cannot be prevented by medical therapy. Refractory ascites is labeled as diuretic resistant and diuretic intractable. Diuretic resistant ascites does not respond to diuretics while diuretic intractable ascites has complications due to side effects of diuretics.  

Q24a. What is the definition of refractory ascites?

Remarks

Refractory ascites is treated by repeated LVP or TIPS.  

Q24b. What is the role of paracentesis for refractory ascites?

Remarks

LVP with administration of albumin is a safe option for patients with recurrent ascites.  

Q24c. What is the role of TIPS in the treatment of refractory ascites?

Remarks

Few randomized controlled trials have been done comparing TIPS with LVP. Rössle et al in their study concluded that the TIPS group had a better transplant-free survival as compared with LVP with similar incidence of HE. Ginès et al concluded that though TIPS was associated with better survival and improvement of HRS, there was increased frequency of HE post-TIPS and that the cost incurred was higher than LVP. Multiple meta-analyses have reported better control of ascites in the TIPS group with increased incidence of HE and no improvement in survival. Salerno et al, in their meta-analysis, suggested that TIPS significantly improved transplant-free survival in patients with refractory ascites. They also showed that the incidence of HE was higher in TIPS group but there was no difference in likelihood of developing first episode of HE.
TIPS should be considered in patients with refractory ascites who are appropriately selected.

Q25. What is the role of tunneled catheters in the treatment of refractory ascites?
Remarks

Tunneled catheters have been used for the treatment of refractory ascites. Tunneled catheters result in surrounding fibrosis, hence reducing the chances of infection.67–70 The long-term patency of tunneled catheters is good but the incidence of infection is high in catheters which have been in place for more than 3 months.69,70 Due to chances of infection, prophylactic antibiotics need to be administered.

Q26. What is the role of peritoneovenous shunting in refractory ascites?
Remarks

Peritoneovenous shunt is also known as Denver shunt. This surgical shunt was effective in decreasing ascites on comparison with medical management with no survival benefit. The associated blockage of the shunt was a recurrent problem. This procedure is rarely performed nowadays.67,68

Q27. What is the treatment of acute variceal bleeding?
Remarks
Pharmacotherapy and endoscopic therapy are the first line of treatments in acute variceal bleeding.19,71

Q28a. What is the role of TIPS in treatment of acute esophageal variceal bleeding?
Remarks

TIPS is used in the treatment of acute variceal bleeding following failure of pharmacotherapy and endoscopic therapy. TIPS has been found to immediately stop hemorrhage in >90% of patients.72,73 Despite cessation of bleeding, the mortality in these patients is still high and outcomes are dependent upon CP score and MELD score.73–75

Q28b. What is the role of early pre-emptive TIPS after esophageal variceal bleeding?
Remarks
Early TIPS means TIPS performed within 72 hours of an esophageal variceal bleed. Multiple randomized control studies concluded that early TIPS was associated with better survival than the pharmacotherapy-endoscopic intervention group.76,77 Early TIPS is associated with reduced risk of treatment failure and re-bleed in addition to reduced chances of developing ascites or worsening of ascites.78

Q28c. What is the role of TIPS in secondary prophylaxis of esophageal variceal bleed?
Remarks
Pharmacotherapy and endoscopic therapy are the treatment of choice for patients with bleeding outside the window of early TIPS. TIPS is more likely to prevent re-bleed than pharmacotherapy or endoscopic intervention in patients who have had multiple episodes of re-bleeding or are at a high risk of variceal hemorrhage.79 Multiple studies, however, have shown that HE is more in patients with TIPS with similar survival benefit. TIPS is more likely to be beneficial in CP Class C patients as compared with endoscopic treatment.79,80

Q29. What is the treatment of acute gastric variceal bleeding?
Remarks

Endoscopic therapy and pharmacotherapy are used in the initial management of gastric variceal bleeding. In patients with bleeding gastroesophageal varices type I (GOV1), cyanoacrylate injection is the first line of treatment.80

Q30. What is the role of TIPS in the treatment of acute gastric variceal bleeding?
Remarks

Gastric varices bleed less frequently but the risk of mortality is high if bleeding occurs. TIPS was found to be effective in controlling acute hemorrhage in bleeding gastric and esophageal varices.81 Studies show conflicting outcomes for re-bleed, hospital stay, and morbidity in patients undergoing TIPS versus endoscopic therapy.81–83 Patients with TIPS are likely to have HE as a side effect and may not be well tolerated in patients with poor hepatic reserve. TIPS is used in the treatment of GOV type 2 and IGVs type 1. All large gastric collaterals should be obliterated at the time of performing TIPS. Embolization with either coils or sclerosing agents (cyanoacrylate) can be done depending on the size of the gastric collaterals.84

Q31. What is the role of BRTO in gastric variceal bleed?
Remarks

BRTO is highly effective in the treatment of gastric varices and reduces the re-bleeding rate. BRTO increases the portal flow and may help in transient improvement in the liver synthetic functions; however, it may cause worsening of esophageal varices in 30% cases.84–86

Q32. What is the advantage of BRTO over TIPS in the treatment of gastric varices?
Remarks

BRTO is equally effective as TIPS in the treatment of gastric varices and reduces the re-bleeding rate with relatively low complications in comparison to TIPS.87 BRTO may result in the improvement of hepatic reserve and HE but there can be worsening of ascites due to worsening PH.84–88 TIPS reduces portal pressure and hence is very effective in controlling esophageal variceal bleed. However, gastric varices are a low-pressure system and bleed at a lower pressure unlike esophageal varices so lowering pressure in a low-pressure system may not be very effective.89,90 BRTO leads to complete obliteration of all gastric varices and hence is very effective in controlling gastric variceal bleed.83–86 However, BRTO increases the portal flow and as a result may cause worsening of esophageal varices.85,86,88

Q33. What is the role of BRTO in HE?
Remarks

Studies show conflicting outcomes for re-bleed, hospital stay, and morbidity in patients undergoing TIPS versus endoscopic therapy.81–83 Patients with TIPS are likely to have HE as a side effect and may not be well tolerated in patients with poor hepatic reserve. TIPS is used in the treatment of GOV type 2 and IGVs type 1. All large gastric collaterals should be obliterated at the time of performing TIPS. Embolization with either coils or sclerosing agents (cyanoacrylate) can be done depending on the size of the gastric collaterals.84
BRTO leads to the closure of portosystemic shunt and hence directs the mesenteric flow toward the liver and avoids portosystemic mixing. This helps in detoxification of ammonia produced in gut, thus helps in treating HE due to portosystemic shunts.

Q34. What is the definition of hepatic hydrothorax?

Remarks
Hepatic hydrothorax is the presence of recurrent pleural effusion in a cirrhotic patient in the absence of pleural or cardiovascular disease. It is more common on the right side. It may cause respiratory failure.

Q35. What is the first line of treatment of hepatic hydrothorax?

Remarks
Pharmacotherapy may be used in the treatment of hepatic hydrothorax. Octreotide and terlipressin have been used with limited success.

Q36. What is the treatment of refractory hydrothorax?

Remarks
a. Pleural thoracocentesis: Repeated aspiration of pleural fluid may be needed. Not more than 1 L of pleural fluid should be aspirated in a single session due to risk of re-expansion pulmonary pneumonia.

b. Tunneled pleural catheters: Presence of drains in the pleura for short duration may be less likely to cause infection but have been associated with pain at the site and frequent occlusion. It can be used as a bridge before TIPS and liver transplant.

c. Pleurodesis: Instillation of an irritant within the pleural cavity causes inflammation and adhesion of the two layers of the pleura. Various chemicals used are tcalc, tetracycline, doxycycline, bleomycin, and betadine. The procedure may be done by instillation of sclerosant via a canula or thoracoscopy with or without video nassistance.

d. TIPS: TIPS has been used effectively to treat hepatic hydrothorax with success.

Q37. What is HRS and how is it treated?

Remarks
Hepatorenal syndrome (HRS) is defined as progressive renal failure in patients with cirrhosis. It is treated by administering vasoconstrictor therapy (Terlipressin) and volume expansion by albumin as a first-line therapy.

Q38. Does TIPS have a role in the treatment of HRS?

Remarks
TIPS has limited success in HRS type 1 despite improvement in renal function as patients usually have a severe liver disease. Patients with type 2 HRS have shown an improvement in renal function after TIPS. Since renal dysfunction is one of the causes of ascites in type 2 HRS, TIPS was found to be beneficial in control of ascites also.

Q39. What is the clinical presentation of BCS?

Remarks
BCS presents with abdominal pain and distension due to ascites, lower limb edema and abdominal wall collaterals. It may be acute, subacute or chronic with acute being associated with rapid deterioration. Few patients are asymptomatic and asymptomatic cases usually have large collaterals. BCS should be suspected in patients with acute or chronic liver disease in whom common causes of liver disease have been ruled out.

Q40. How is BCS diagnosed?

Remarks
US is the initial imaging modality and has a sensitivity of more than 75% in diagnosing BCS. Liver is enlarged and congested in acute BCS with thrombus in hepatic veins. Chronic thrombosis or narrowing of the hepatic veins may be seen in chronic BCS with the development of comma-shaped intrahepatic, venovenous, bridging collaterals. Multiphasic CT and MRI can be done for confirmation of diagnosis if the US is equivocal and if an intervention is planned.

Q41. What is the pharmacological treatment of BCS?

Remarks
Long-term treatment with low molecular weight heparin and vitamin K antagonists are used for the treatment of BCS.

Q42. What interventional treatments are possible for BCS?

Remarks
Symptomatic BCS may be treated by restoration of hepatic venous outflow or by creating a portosystemic shunt. Hepatic venous outflow is obstructed at the level of hepatic veins or supra-hepatic IVC. The aim of venoplasty/stenting is to decongest the liver and restore normal pathway of venous drainage. Venoplasty using serial balloon dilatation is used for short segment stenosis. If the narrowing does not resolve, a stent should be placed. Long-term anticoagulation should be continued. Treatment of obstruction causes reduction in congestion and hence the liver stiffness which can be measured by TE.

Q43. When is TIPS/direct intrahepatic portosystemic shunt (DIPS) used as a therapeutic option in BCS?

Remarks
TIPS/DIPS is used in symptomatic BCS, in whom venoplasty/stenting is not feasible. TIPS/DIPS has shown excellent long-term outcome with improved long-term outcome and improved survival. TIPS is better than surgical procedures in terms of morbidity and mortality. In a study, Mukund et al compared the clinical improvement and survival in patients with anatomical recanalization and DIPS creation. The clinical improvement and survival in both
groups were similar, whereas improvement in liver functions was better in anatomical recanalization group.\textsuperscript{109}

**PART 2**

**Q1. What are the indications of TIPS?**

Remarks

**Indications of TIPS are**\textsuperscript{79,110–113}:

- Acute esophageal variceal bleeding.
  - Salvage procedure in acute variceal bleeding
  - Early TIPS after esophageal variceal bleeding
  - Secondary prophylaxis of esophageal variceal bleed
- Acute gastric variceal bleeding in GOV type 2 and IGV type 1.
- Refractory ascites.
- Refractory hydrothorax.
- Hepatorenal syndrome.
- BCS.

**Q2. What are the absolute contraindications of TIPS?**

Remarks

**Absolute contraindications of TIPS are**\textsuperscript{79,110–113}:

- Congestive cardiac failure.
- Severe tricuspid regurgitation.
- Severe pulmonary hypertension.
- Sepsis.
- Unrelieved biliary obstruction.

TIPS placement increases the volume of blood returning to the heart, thereby increasing the right heart pressure, and exacerbates pre-existing heart failure. Sepsis and unrelieved biliary obstruction may present with worsening of liver functions tests post-TIPS.\textsuperscript{107,108}

**Q3. What are the relative contraindications of TIPS?**

Remarks

**Relative contraindications of TIPS are**\textsuperscript{79,110–113}:

- Severe coagulopathy.
- Severe thrombocytopenia.
- Encephalopathy.
- Moderate pulmonary hypertension.
- Centrally located liver mass.

Relative contraindications are usually conditions in which there is an anatomical hindrance to placement of the TIPS stent. Severe coagulopathy/thrombocytopenia can be managed by the administration of fresh frozen plasma and platelet infusion.

**Q4. Who should perform TIPS and where should it be done?**

Remarks

TIPS should be performed by an experienced interventional radiologist, and it should be performed in a tertiary care hospital.\textsuperscript{79} The decision for TIPS should be taken by a team of interventional radiologists, hepatologists, and transplant surgeons. Cardiologists for assessment and management of cardiac functions pre- and post-TIPS should also be available.\textsuperscript{79,113}

**Q5. What are the investigations performed prior to TIPS procedure?**

Remarks

Liver function tests, renal function tests, coagulation profile, CP score, MELD, and echocardiography are to be done prior to the procedure. Since TIPS causes altered hemodynamics of the right-sided cardiac chambers, a pre-procedural cardiac evaluation is essential prior to TIPS procedure.\textsuperscript{79,114,115} CP Class C, serum bilirubin > 3 mg/dl, alanine aminotransferase > 100 IU/L, and pre-TIPS encephalopathy are independent predictors of mortality after TIPS.\textsuperscript{79,115} MELD score is better than CP score to predict 30-day mortality and those with MELD score ≥ 18 have a higher mortality.\textsuperscript{79} However, MELD score was not found to predict long-term outcomes.\textsuperscript{115}

**Q6. What imaging should be performed prior to TIPS?**

Remarks

US Doppler along with cross-sectional is important for the assessment of the hepatic veins, IVC, and the portal vein.\textsuperscript{116} Imaging helps in ruling out contraindications and reviewing the anatomy to recognize favorable anatomy.\textsuperscript{116}

**Q7. What is the preferred route for performing TIPS?**

Remarks

Right internal jugular route is the preferred route for performing TIPS.\textsuperscript{111} A meta-analysis by Hung and Lee showed that the use of two-dimensional US was found to be better than blind technique. There was a significant reduction in the complications and the puncture being performed in the first attempt.\textsuperscript{112}

**Q8. Which hepatic vein should be chosen for performing TIPS?**

Remarks

Right hepatic vein is the preferred vein for performing TIPS.\textsuperscript{111,116} However, patients with deformed liver due to atrophy hypertrophy complex may be opted for alternate and more appropriate hepatic vein.\textsuperscript{116}

**Q9. Why should portal vein be punctured under US guidance?**

Remarks

Use of real-time US significantly reduces the radiation dose and fluoroscopy time. Real-time US also prevents other complications by reducing the chances of extracapsular puncture and accidental puncture of bile ducts/hepatic artery.\textsuperscript{117–119} Intravascular ultrasound (IVUS) has recently been used for the guidance of portal vein puncture. The IVUS transducer is placed in the IVC via the right femoral approach and guidance is provided for the puncture of the portal vein for TIPS/DIPS.\textsuperscript{119} In a comparison with conventional TIPS, Pillai et al observed that IVUS-guided puncture of the portal vein showed significant reduction in portal vein access time in addition to reduction in needle pass-related complications and radiation dose.\textsuperscript{120,121}
Q10. Why are covered stents preferred for TIPS?

Remarks
Covered stents are less prone to occlusion as the PTFE covering prevents pseudo intimal hyperplasia and acute thrombosis which is mostly related to bile intravasation into the stent. Studies have shown covered stents to have a better patency and survival rates in patients with variceal bleeding and ascites.

Q11. What is the desired portosystemic gradient post-TIPS?

Remarks
Portosystemic gradient should be measured before and after the procedure. The target of TIPS creation is to reduce the portosystemic gradient to less than 12 mm Hg. Reduction of HVPG to ≤ 12 mm Hg is associated with the resolution of varices. Reduction of HVPG >20% from the baseline results in reduced risk of variceal re-bleed, ascites, and mortality. Pressures should be measured in the portal vein and the IVC adjacent to the TIPS stent.

Q12. What should be done if post-TIPS portosystemic gradient does not reduce below 12 mm Hg?

Remarks
In patients with acute variceal bleed, if the portosystemic gradient across TIPS persists to be high (> 12 mm Hg), then additional embolization of varices arising from the splenoportal axis may be done to stop the ongoing bleed and prevent variceal re-bleed. Studies and meta-analysis have shown a reduced re-bleed rate in patients undergoing additional variceal embolization.

Q13. Can TIPS be performed in patients with PVT?

Remarks
PVT and cavernoma formation are relative contraindications of TIPS. TIPS may be performed if anticoagulation therapy fails in resolving PVT. Patent right and left portal vein with partial thrombosis of the main portal vein had a better technical success than extension of thrombosis in right or the left portal vein. TIPS may be performed in PVT with cavernoma formation in patients with severe PH who have not responded to medical treatment.

Q14. What are the complications of TIPS?

Remarks
14a. HE is one of the major complications of TIPS. Increasing age, high CP score, higher creatinine values, low sodium, and low albumin levels are independent predictors of post-TIPS encephalopathy. Treatment is by medical management and TIPS reduction may be contemplated if medical therapy fails.

14b. Puncture-related complications are liver capsule puncture, haemobilia, or biliary fistula.

The complications can be minimized by using US guidance for puncture and avoiding artery/bile ducts. Minimal needle passes should be taken. Non-target puncture does not cause significant clinical consequences.

14c. Stent-related complications are TIPS-itis, stent thrombosis, stent stenosis, and stent migration. TIPS-itis is bacterial colonization of the TIPS stent which is managed by broad-spectrum parenteral antibiotics. TIPS-itis tends to be recurrent.

TIPS thrombosis/stenosis can be treated by angioplasty and administration of anticoagulants. If there is recurrent thrombosis/stenosis, hypercoagulable states should be ruled out.

14d. Post-TIPS hepatic failure may be due to (a) diversion of portal blood via TIPS, (b) occlusion of hepatic artery by stent, and (c) occlusion of hepatic vein by covered parts of the stent.

Post-TIPS hepatic failure is more likely to occur in patients with poor pre-procedure hepatic reserve. Contrast-enhanced CT can assist in the diagnosis of arterial or hepatic vein occlusion and absence of occlusion suggests dysfunction due to diversion of portal flow. In these cases, shunt reduction or occlusion may be attempted.

Q15. What are the indications for BRTO?

Remarks
Bleeding gastric varices and HE are indications for BRTO. BRTO may be used for bleeding gastric varices with large gastrorenal/splenorenal shunts.

HE is caused by portosystemic shunting resulting in high ammonia levels and occluding these shunts may improve encephalopathy.

Q16. What are the contraindications for BRTO?

Remarks
Coagulopathy is usually a manifestation of associated liver disease. Risk-versus-benefit ratio should be calculated and BRTO may be performed in an actively bleeding patient in whom endoscopic treatment has failed. In case of portal venous thrombosis, the gastrorenal shunt may be the only pathway to the splanchnic circulation but there may be increased portal flow through the periportal collaterals. Patients with gastric varices, isolated splenic vein thrombosis, and splenomegaly may be treated by splenic artery embolization with or without BRTO. Since there is increased flow through the portal vein and the portal pressure, there are chances of recurrence or bleeding of existing esophageal varices.

Q17. Which imaging is needed prior to BRTO?

Remarks
Multiphasic CECT is needed to evaluate various veins. The main portal vein, the presence and sizes of gastrorenal/splenorenal shunts, any other shunts need to be thoroughly examined in the CT. Transdiaphragmatic shunts also need to be kept in mind.
Q18. What is the preferable access for performing BRTO?
Remarks
Femoral venous approach is the most widely used access for BRTO. However, depending on the anatomy and orientation of left renal vein and gastrolieniorenal shunt as evaluated on pre-procedure CT, appropriate access—femoral or jugular—may be taken.

Q19. Which sclerosant is safe to use for BRTO?
Sodium-tetradecyl-sulfate is one of the safest and most widely used sclerosants for BRTO.
Remarks
Ethanolamine oleate (EO) was the initial sclerosant used and described for BRTO. But EO was associated with renal complications. However, recent studies have proved beyond doubt the safety and efficacy of sodium-tetradecyl-sulfate in BRTO.

Q20. Which balloon should be used and what is the ideal balloon dwell time?
Compliant balloon catheter should be used, and the shunt should be occluded with balloon for at least 4 to 6 hours.
Remarks
Compliant balloon should be used for occluding the shunt for performing BRTO as it provides a better and non-traumatic occlusion. Moreover, it may be used for occluding large shunts for which plugs may not be available. After occluding the shunt with the compliant balloon, venogram is performed to look for adequate occlusion of shunt. Once the tight occlusion is achieved, sclerosant in the form of foam is injected to fill the shunt and varices. Balloon dwell time should be 4 to 6 hours as this provides adequate time for thrombus formation within the shunt and the varices. However, before the removal of balloon catheter, complete thrombosis within the shunt should be ascertained and balloon should be removed carefully. Also, keeping the balloon for 4 to 6 hours is associated with lesser patient discomfort and lesser chances of infection.

Q21. What is the end point of sclerosant administration?
Remarks
The end point of sclerosant administration is filling of the shunt as well as the target varices with the sclerosing agent and just visualization of the afferent vein.

Q19. What are the modifications in BRTO to make it quick?
PARTO has been proposed and shown to be a quick technique and devoid of complications associated with rupture of balloon.
Remarks
PARTO has been conceptualized with an idea of replacing the balloon catheter with vascular plug, thus reducing the balloon dwell time (4–6 hours) and making the procedure very fast.

Further, PARTO is free of complications related to balloon rupture and associated pulmonary embolism. In PARTO, vascular plug and a catheter are placed side by side within the shunt with catheter tip proximal to the plug. The plug is deployed and after confirming adequate closure of the shunt, gelfoam slurry is injected proximal to the plug through the catheter placed by the side of plug. Gelfoam slurry is injected to completely fill the varices and the catheter is removed.

Q20. What are the complications of BRTO/PARTO?
Remarks
Exacerbation of ascites/pleural effusion, exacerbation of esophageal varices and gastropathy are due to increased portal flow and resulting increased portal pressure. Portal venous thrombus was classified as high attenuation, combined and low attenuation by Cho et al. High attenuation thrombus were thought to be due to iodized oil. They hinted that high attenuation thrombus was not of much significance but low attenuation thrombus could progress to complete occlusion.

Declaration of Patient Consent
The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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