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Pediatric portal hypertension:
A review for primary care

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Abstract: Pediatric portal hypertension management is a team approach between the patient, the patient's family, the primary caregiver, and specialty providers. Evidence-based practice guidelines have not been established in pediatrics. This article serves as a review for the primary care NP in the management of pediatric portal hypertension, discussing the etiology, pathophysiology, and clinical presentation of pediatric portal hypertension, diagnostic tests, and treatment and management options.

The NP can play a key role in pediatric patients with portal hypertension. Subtle signs and symptoms during a routine physical exam may provide clues suggesting significant liver disease and prompt referral to a specialist. This can either be a pediatric gastroenterologist trained in the management of pediatric portal hypertension or a pediatric hepatologist. Depending on the geographic location and a specialist's ability to manage pediatric portal hypertension, either referral is appropriate.

These specialists can be found in children's hospitals that are affiliated with a teaching university or medical school located in major cities. Some may even have satellite offices where routine follow-up can be done locally, and any procedure or surgery (if warranted) would be performed at the affiliated children's hospital.

Once the diagnosis of pediatric portal hypertension is confirmed, a collaborative management plan between the

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patient, the patient's family, the NP, and specialist will ensure proper care and follow-up going forward. This article discusses the etiology, pathophysiology, and clinical presentation of pediatric portal hypertension, diagnostic tests, and treatment and management options.

Treatment and management of children with portal hypertension have not been well studied, and there are no current guidelines. In adults, evidence-based approaches in treating and managing portal hypertension are well studied in the literature. In May 2010, the Baveno V Consensus Workshop on the methodology of diagnosis and therapy in portal hypertension was held; it was comprised of international experts in the field who reviewed portal hypertension, the current evidence, and best practices.[1] In 2011 at The Children's Hospital in Pittsburgh, international panels of experts convened to review and adapt the Workshop's findings, which were then published.[1] In 2009, experts gathered at the American Association for the Study of Liver Diseases' (AASLD) annual meeting to discuss primary prophylaxis in children with variceal hemorrhage in children with portal hypertension.[2] The findings from both meetings are discussed in this article.

Etiology

Portal hypertension is a clinical manifestation of cirrhotic (scarred) liver disease; however, it can arise from other etiologies not associated with cirrhosis. This article focuses on noncirrhotic pediatric portal hypertension, which is not well documented in the literature.

Noncirrhotic etiologies of portal hypertension are classified as prehepatic, hepatic, and posthepatic (see *Causes of pediatric portal hypertension*).[3] Etiologies and further workup are managed by the specialist. The NP plays a role in initial recognition and health maintenance of pediatric patients with portal hypertension.

The most commonly identified cause of pediatric portal hypertension is extrahepatic portal vein obstruction (EHPVO). The etiology of EHPVO is poorly understood, although studies have identified predisposing factors, such as history of umbilical catheterization, dehydration, trauma, or a hypercoagulable state. More than 50% of pediatric cases are idiopathic.[4]

Pathophysiology

Portal hypertension is defined as a pathologic increase of pressure of the portal system. Due to the presence of

Causes of pediatric portal hypertension[3]

Location of lesion	Diagnostic group	Examples
Intrahepatic	Cholestatic disease	• Biliary atresia • Progressive familial intrahepatic cholestasis • Primary sclerosing cholangitis • Cystic fibrosis-related liver disease • Intestinal failure-associated liver disease
	Hepatocellular disease	• Autoimmune hepatitis • Chronic viral hepatitis B • Chronic viral hepatitis C • Alpha$_1$-antitrypsin deficiency • Nonalcoholic fatty liver disease
	Fibrotic disease	• Congenital hepatic fibrosis • Caroli disease
Prehepatic	Portal vein occlusion	• Portal vein thrombosis • Tumor (infiltration by hepatoblastoma, hepatocellular carcinoma, or compression by large focal nodular hyperplasia)
	Nodular regenerative hyperplasia	• Drug therapy (6-thioguanine and azathioprine) • Turner syndrome
	Portal venopathy or portal sclerosis	• Schistosomiasis • Idiopathic cause • HIV infection • Cystic fibrosis liver disease
Posthepatic	Hepatic vein obstruction	• Budd-Chiari syndrome • Inferior vena cava obstruction • Congestive heart failure • Veno-occlusive disease (sinusoidal obstruction syndrome)

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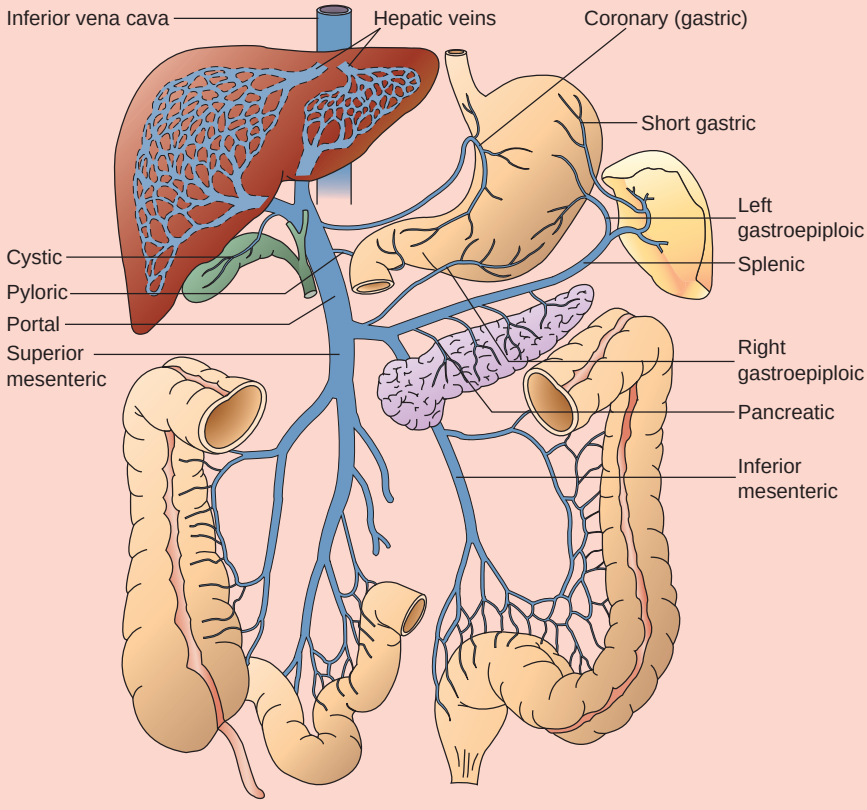
Portal circulation

Blood from the GI tract, spleen, and pancreas travels to the liver through the portal vein before moving into the vena cava for return to the heart.



Source: Porth CM. *Essentials of Pathophysiology: Concepts of Altered Health States.* 4th ed. Philadelphia, PA: Wolters Kluwer Health/Lippincott Williams & Wilkins; 2015:725.

EHPVO, this blockage causes blood to backflow into connecting organs, such as the spleen (causing splenomegaly), esophagus, and gastrointestinal (GI) tract (causing dilated blood vessels).[5] (See *Portal circulation.*)

Clinical presentation

Portal hypertension is a clinical diagnosis identified through history and physical exam. The two most common clinical manifestations of pediatric portal hypertension that may prompt referral are upper GI bleeding (UGIB) and splenomegaly.[5] EHPVO may present from age 6 to adulthood but is primarily a childhood disorder.[6]

In children, UGIB is most commonly the initial clinical manifestation of EHPVO. Esophageal varices occur in 90% to 95% of patients, and gastric varices occur in 35% to 40%.[5] Seventy-nine percent of children with EHPVO are anticipated to have at least one episode of UGIB in their lifetime.[5] Variceal bleeding in children is often seen following an upper respiratory infection, fever, or aspirin ingestion.

Throughout the duration of the illness, coughing and sneezing create abdominal pressure; fever increases cardiac output; and the use of nonsteroidal anti-inflammatory drugs or aspirin (when medically indicated) to treat symptoms can create ulcers and contribute to the rupture of varices. In addition, long-standing gastroesophageal reflux can contribute to erosions over varices, which could result in bleeding.[5]

Splenomegaly is often first discovered during routine physical exam.[5] Children with enlarged spleens are often first referred to a hematologist to rule out any possible hematologic processes, especially if leukopenia is present. Once hematologic causes are ruled out, referral to a pediatric gastroenterologist or hepatologist is appropriate.[7] Clinical findings may include growth failure; one prospective study showed that 50% of children with EHPVO had growth retardation compared with healthy children who did not have EHPVO.[5]

Diagnostic tests

Diagnostic lab tests that the NP can obtain as initial workup include a complete blood count (CBC) with differential and

platelet count (CBC with platelets), hepatic function panel, gamma-glutamyl transpeptidase, magnesium, phosphorus, and international normalized ratio. Lab findings of pediatric patients with portal hypertension due to EHPVO have normal or near normal liver function tests in the absence of underlying functional liver disease. Common lab findings include leukopenia, anemia, and thrombocytopenia from splenomegaly. In addition, anemia may be due to chronic blood loss from variceal bleeding.[5,6]

Treatment of pediatric portal hypertension includes endoscopic treatment, drug therapy to reduce portal pressures, and surgery.

Doppler ultrasonography is the most useful diagnostic tool for differential diagnosis. The aspect of hepatic parenchyma and the liver capsule, the patency of the portal vein or its replacement by a cavernoma, the flow pattern of the hepatic veins and hepatic artery, and the presence of splenomegaly or liver atrophy are important elements for the diagnosis and staging of the patient's condition.[1,6] For the diagnosis of EHPVO, ultrasonography with Doppler has a sensitivity and specificity above 95%.[5]

Depending on the resources of the practice, NPs may obtain an ultrasonography with Doppler before a referral to the specialist. Doppler ultrasonography helps to assess anatomy and blood flow and rule out the presence of any masses. Common findings on abdominal ultrasound in the setting of portal hypertension may include splenomegaly, the presence of collaterals (new veins), and possible reversal of portal vein blood flow (more severe cases).[3] Patients with EHPVO have an abdominal ultrasound showing obstruction of the main portal vein with cavernous transformation. This appears as an irregular tangle of vessels near the hilum of the liver, which is a sign of chronicity.[5]

If the child has had previous blood work and/or imaging, the parents should be instructed to bring copies of reports and imaging on a compact disc to the initial consultation with the specialist. A positive history and physical, blood work, and Doppler ultrasonography are a sufficient workup that the NP can initiate prior to referral to a pediatric gastroenterologist or hepatologist.

Additional workup that the specialist may prescribe is a contrast-enhanced computed tomography or magnetic resonance angiography.[4] Both are useful for assessing the extent of thrombosis and can serve as an anatomical road map if surgery is needed.[4,5] A liver biopsy is standard practice for the diagnosis for EHPVO because the liver parenchyma is usually normal.[1] A liver biopsy would be warranted if there was suspicion of other underlying liver disease.[1,5]

Diagnosis of portal hypertension can be further confirmed by measuring portal pressures. This practice is invasive, requires anesthesia, and is not a common diagnostic tool used in pediatrics. Portal hypertension is defined as a portal pressure greater than 12 mm Hg or gradient greater than 6 mm Hg to 7 mm Hg. Normal portal pressure is between 5 mm Hg and 10 mm Hg.[8] Measuring portal pressure gradients is invasive and requires catheterization of the jugular or femoral vein with measurement of right atrial pressure, free hepatic venous pressure (FHVP), and wedged hepatic venous pressure (WHVP).

The hepatic venous pressure gradient is the difference between WHVP and FHVP.[8] If a pediatric patient is going under anesthesia for a different purpose, portal pressures may be measured for a baseline, but this is not a common practice in diagnosis and management. A retrospective single-center study showed that this practice is safe and feasible in children with acute and chronic liver disease, including those who are critically ill; however, further research is needed regarding its use as a diagnostic tool after initial presentation.[9]

Treatment and management

Treatment measures for pediatric portal hypertension include endoscopic treatment, drug therapy to reduce portal pressures, and surgery.[10] Treatment and management are determined by the underlying cause of portal hypertension and the expertise of the specialist.[1,5]

Endoscopic treatment. A surveillance esophagogastroduodenoscopy (EGD) may be performed at baseline to stratify risk for variceal bleeding. EGD is the best available test for the diagnosis for varices.[3] There are two types of endoscopic modalities: endoscopic sclerotherapy (EST) and endoscopic variceal ligation (EVL), also known as endoscopic band ligation. Both are highly effective in controlling acute variceal bleeding in over 90% of cases as well as in eradication of variceal bleeding.[5] The use of beta-blockers, EST, and/or EVL are considered primary prophylaxis treatments for variceal bleeding in adults; however, due to the lack of controlled pediatric data, primary prophylaxis remains controversial, and practices among centers vary significantly.[1,3]

EST is the use of an endoscope and injecting sclerosing agents, such as ethanolamine oleate, inside or around varices.[5,11] Children with EHPVO who received EST for variceal bleeding showed low recurrence rates.[5] Potential complications associated with EST include esophageal

ulcerations and strictures, esophageal perforation, motility disorders, decreased low esophageal sphincter pressure, and gastroesophageal reflux disease.[5] EST was shown to be useful even in very small children as young as 5 months weighing 12 lb (5.5 kg).[1,8]

EVL is performed via an upper endoscopy and uses bands to tie off varices to prevent further bleeding. In the past 10 years, EVL has been more widely used and found to be more superior to EST as far as efficacy, safety, and degree of standardization in adults and children.[1,3] However, it is not always feasible because there currently are no devices small enough that can be used in pediatric patients. Therefore, EST remains the only option for young children.[5] EVL is the recommended therapy for acute esophageal variceal bleeding.[1] Recurrence of bleeding is lower in patients treated with EVL because the varices are eradicated in fewer endoscopic sessions.[5]

There are very little data on the diagnosis and grading of esophageal varices in children. The current scoring system has been adopted from adult practice; however, it has not been validated in the literature.[1,2,11] One retrospective study conducted in a single academic hospital setting found that the majority of patients with noncirrhotic portal hypertension did well long term without surgical shunt placements, and treatment focused mainly on surveillance and treatment of varices.[12] However, this practice has not been well studied and reviewed in the literature.[12]

Drug therapy to reduce portal pressure. The use of nonselective beta-blockers (propranolol or nadolol) should be avoided in children while evidence is awaited regarding appropriate dosing, efficacy, and safety.[1] However, some specialists may use them to reduce hepatic venous pressure gradient by decreasing cardiac output ($beta_1$-receptor antagonism) and inducing splanchnic vasoconstriction ($beta_2$-receptor antagonism).[5] The data for using beta-blockers for the treatment for children with portal hypertension are scarce, deriving mainly from case series with a limited number of patients. Adverse reactions from the use of beta-blockers in children include significant hypotension due to suppression of the normal tachycardic response and hypovolemia due to poor ability to increase stroke volume to support cardiac output, bronchospasm, and hypoglycemia.[2,5] It is important for the NP to be aware of indications for a beta-blocker in the management of portal hypertension and the potential adverse reactions.

Surgery. Surgical shunts are usually reserved for patients with thrombocytopenia and recurrent bleeding when liver transplant is not a consideration and endoscopic therapy is ineffective.[7] Surgery is performed at a children's hospital that the specialist is affiliated with.

The ideal surgery for patients with EHPVO is a meso-Rex bypass shunt, which connects the junction of the superior mesenteric and splenic veins to the left portal vein using an internal jugular jump graft.[1,5] This procedure bypasses the obstruction and restores nutritive blood flow to the liver. If the meso-Rex cannot be performed due to unsatisfactory anatomy, a distal splenorenal shunt should be considered if EST or EVL did not adequately control variceal bleeding.[1]

Patients being considered for surgical interventions should be immunized in advance to include protection from meningococcus, *Haemophilus influenzae* type B, and pneumococcus (pneumococcal 13-valent conjugate vaccine and pneumococcal vaccine polyvalent given 8 weeks apart). This is congruent with the American Academy of Pediatrics' recommendations for vaccinating patients with chronic liver disease or cirrhosis.[13,14] There is a potential for splenic injury during shunt surgery due to the anatomic location, and an emergency splenic embolization may be performed; therefore, proper preoperative immunization is important.[1]

Two common clinical manifestations of pediatric portal hypertension that may prompt referral are upper GI bleeding and splenomegaly.

Transjugular intrahepatic portosystemic shunt (TIPS), which may be a good technical option in EHPVO, is rarely if ever indicated as a means of secondary prophylaxis in variceal hemorrhage for portal hypertension in children. Main indications are refractory or recurrent variceal bleeding and diuretic-resistant ascites in adults.[5] Placement of TIPS stents can prevent future successful meso-Rex bypass by permanently blocking access to the intrahepatic vein if it is open.[1] However, this practice is rarely used in pediatrics, and there is no supporting evidence in the literature on its efficacy.

Possible complications

Reported complications from portal hypertension include hemorrhage from varices, ascites, hepatopulmonary syndrome, portopulmonary hypertension, and hepatic encephalopathy.[3] Variceal bleeding is the most serious complication of portal hypertension, which can occur from venous collaterals in the stomach or esophagus. Varices and ascites are seen when portal pressure is 12 mm Hg or greater.[8] This is not a subtle finding, as there is a 30% mortality with variceal bleeding.[8]

Variceal bleeding can occur with or without the above treatments at any time. Patients with active variceal bleeding should be directed to the closest ED because this constitutes a medical emergency. Upon arrival, the child's parent or guardian should tell the ED provider that the child has UGIB due to portal hypertension. This will guide the ED in management and stabilization. Octreotide is a vasopressin analogue (used off-label for variceal bleeding) that is effective in stopping acute variceal bleeding in 95% of cases when administered as an infusion. After stabilization with octreotide, acid-blocking agents (for GI prophylaxis), and blood products (red blood cells and/or platelets), the patient should have an EGD performed within 24 hours.[1]

Children with an enlarged spleen should refrain from contact sports and may need to wear a spleen guard for prevention of splenic rupture.

Implications for advance practice nursing

It is important that both the NP and specialists stay current on guidelines and recommendations in the management and care of pediatric portal hypertension. Most centers follow guidelines from the AASLD. Education of the family regarding portal hypertension is important (see *Portal hypertension: A guide for parents*). In addition, limiting excessive salt and water intake to avoid ascites and recognition of UGIB to expedite emergent intervention is clearly a shared charge between the primary care NP and specialist.

A team approach by the NP and specialist is paramount in managing patients with portal hypertension. The NP is typically the gatekeeper who first identifies the initial signs of portal hypertension, such as splenomegaly on physical exam, and plays a crucial role in the initial workup, referral, diagnosis, and management (see *Clinical pathway for referral*).

Children with portal hypertension should receive all routine healthcare maintenance, including childhood

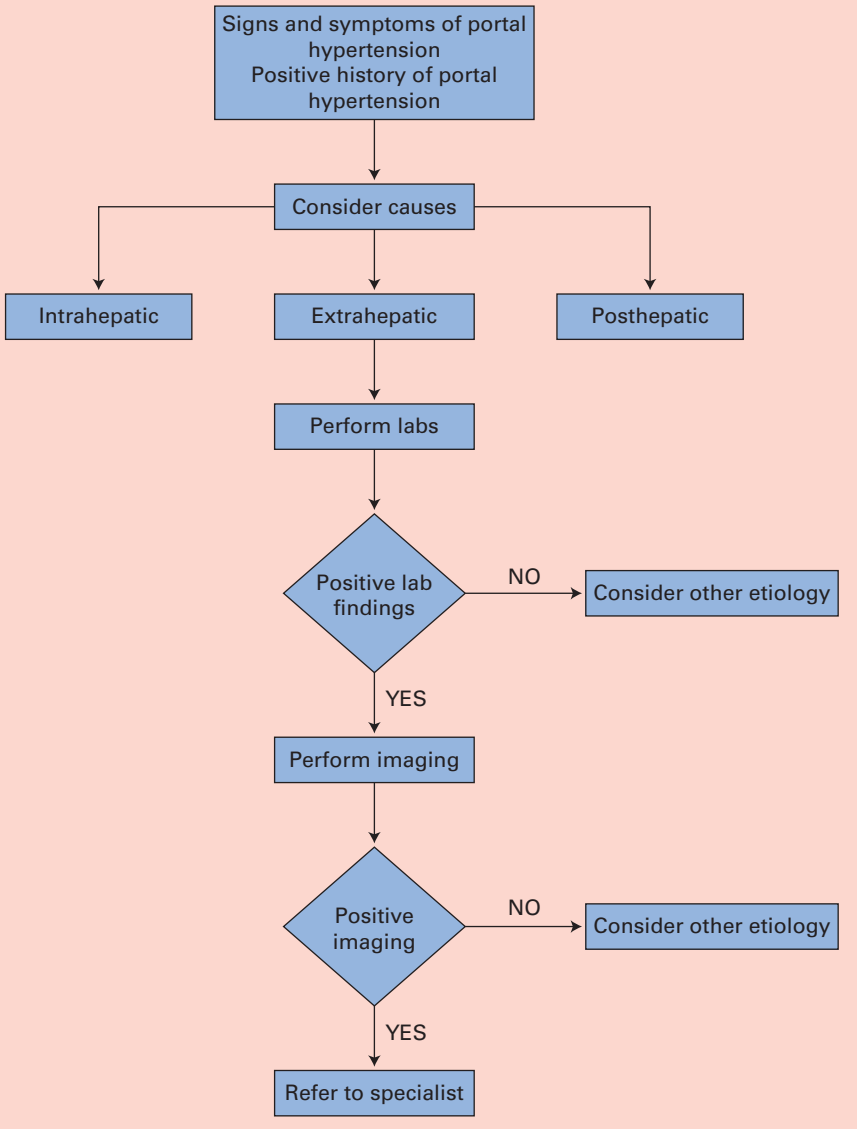
Portal hypertension: A guide for parents

Question	Answer
What is portal hypertension?	Portal hypertension is a high amount of pressure in the liver's blood system. It is not measured with a blood pressure cuff.
How is the diagnosis made?	The child's primary care provider will perform a physical exam, medical history, and blood tests. Depending on the results, a referral to another specialist such as a pediatric gastroenterologist (stomach doctor) or pediatric hepatologist (liver doctor) may be needed for management and treatment.
How is portal hypertension treated?	The child may need to take medicine, have liver imaging and blood tests done, and may have to undergo a procedure that examines the digestive tract (endoscopy). Some children need surgery.
What is the treatment for bleeding?	Symptoms of bleeding include being tired, looking pale, and having shortness of breath. A child may either have a large amount of blood come up from their mouth or in the stool, which may be red or black. This is a medical emergency, and a parent should either call 911 or bring the child to the nearest emergency department. Upon arrival, parents should notify the emergency staff that their child has portal hypertension and what medicines, if any, the child is taking. The child will have a small, flexible tube placed in a vein for hydration (I.V. catheter) and will be monitored. Medicine may also be given through the I.V. catheter. The child may stay overnight for observation, and a thin scope with a light and a camera may be inserted into the stomach (endoscopy) to look for bleeding.
Are there any special safety measures children with portal hypertension should take?	Children with portal hypertension should still see their primary care NP for all routine care including all checkups and vaccinations. If the spleen is enlarged, children may need to refrain from contact sports (football, soccer, baseball, hockey). Children may need to wear a shield over their stomach called a "spleen guard" if they have an enlarged spleen and will be participating in sports.

vaccinations and routine screenings. Children with an enlarged spleen should refrain from contact sports and may need to wear a spleen guard for prevention of splenic rupture.[1] The NP should work closely with the child's school nurse to monitor for changes in clinical status, such as checking vital signs, and help carry out avoidance of contact sports in physical education class if the child has splenomegaly. The school nurse may also be the first responder in the event the child may show signs of a UGIB and aid in getting medical attention.

The specialist will manage surveillance of portal hypertension, such as physical exam, endoscopy, labs, possible beta-blockers, and imaging. Frequency of obtaining labs could be coordinated with the specialist and NP. Children with portal hypertension should eat a healthy, balanced diet. The main management of portal hypertension in children focuses on preventing decompensation, which includes control and prevention of ascites and portal hypertension bleeding.[5] If a child is placed on a beta-blocker or if there is titration in the dose by the specialist, the child may be scheduled for follow-up visits with the NP for heart rate and BP monitoring. Follow-up with the specialist is individualized to each patient. Parents of children with portal hypertension can reach out to the center where the child is being managed for support and support groups that may be available to them locally.

Clinical pathway for referral



Additional research is needed on the management of esophageal varices in children with portal hypertension. Conversely, in adults, treatments have been challenged with a plethora of studies that have been conducted in the Baveno V Consensus Workshop. Most pediatric centers adapt practices to what has been found to be successful in adult studies.[11] Depending on the center's preference and clinical status of the child with portal hypertension, treatments can vary from routine endoscopy to use of beta-blockers as primary prophylaxis and surgical options as secondary treatment. Currently, management relies on expert opinion, low-quality pediatric studies, and the extrapolation of results seen in studies in the adult population. There is a need for high-quality pediatric studies to help guide practice.[11]

Providing optimal care

Understanding the pathophysiology of portal hypertension due to EHPVO in pediatric patients is important to help guide proper management, prevention, and overall outcomes. Effective collaboration between the NP and specialist is key in providing optimal care for a child with portal hypertension. Management of portal hypertension can

include medications, endoscopic and surgical options to ensure a good long-term prognosis, and routine healthcare maintenance, including childhood vaccinations and routine screenings.

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