Prognostic Factors of Transjugular Intrahepatic Portosystemic Shunt and its impact on Health Related Quality of Life in Egyptian Patients with Budd-Chiari Syndrome

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Introduction

Budd described this hepatic disorder in 1845, and **Chiari** added the first pathologic description of a liver with "obliterating endophlebitis of the hepatic veins" in 1899 ***(Roy, 2006).***

Primary Budd-Chiari syndrome is characterized by a blocked hepatic venous outflow tract at various levels from small hepatic veins to inferior vena cava ***(Valla, 2009)***, in absence of right heart failure or constrictive pericarditis ***(Janssen et al., 2003).***

This rare disease affects mainly young adults. Multiple risk factors have been identified and are often combined in the same patient ***(Valla, 2009)***.

This condition is variable in its presentation and natural history and can be life threatening if not diagnosed and treated promptly ***(Vladimir et al., 2005).***

BCS is considered primary or secondary depending on the origin of the obstructive lesion. If obstruction is the result of endoluminal venous lesion like thrombosis, primary BCS is considered. In secondary BCS, the cause originates from neighboring structures like extrinsic compression or tumor invasion ***(Aydinli and Bayraktar, 2007).***

Thrombosis is the major cause of hepatic vein obstruction. The combination of one or more thrombogenic disorders and a triggering factor is necessary for venous thrombosis, particularly hepatic vein thrombosis. Most patients with BCS have an underlying condition that predisposes to blood clotting. Obstruction is mainly caused by primary intravascular thrombosis. At least one hereditary or acquired hypercoagulable state could be identified in 75% of patients; more than one etiologic factor may play a role in 25% of patients ***(Denninger et al., 2000)***

Presentation and manifestations are extremely varied, so that the diagnosis must be considered in any patient with acute or chronic liver disease. Doppler-ultrasound, computed tomography or magnetic resonance imaging of hepatic veins and inferior vena cava are usually successful in demonstrating non-invasively the obstacle or its consequences, the collaterals to hepatic veins or inferior vena cava ***(Valla, 2009)***.

A therapeutic strategy has been proposed where anticoagulation, correction of risk factors, diuretics and prophylaxis for portal hypertension are used first; then angioplasty for short-length venous stenosis or TIPS for long segment occlusion, and ultimately liver transplantation ***(Valla, 2009)***.

Treatment progression is dictated by the response to previous therapy. This strategy has achieved 5-year survival rates approaching 90%. Medium-term prognosis depends on the severity of liver disease. Long-term outcome might be jeopardized by transformation of underlying conditions and hepatocellular carcinoma ***(Valla, 2009)***.

TIPS decompress the liver by creating an alternative venous outflow tract ***(Panagiotou et al., 2007).*** It is particularly useful, either alone or as a bridge to liver transplantation, in patients with an acute presentation such as those with variceal bleeding, and patients with fulminant hepatic failure or chronic illness in whom thrombolysis and angioplasty were unsuccessful ***(Ganger et al., 1999 and Khuroo et al., 2005).***

TIPS may be preferred over surgical shunting because it avoids laparotomy and has less periprocedure mortality and morbidity ***(Senzolo et al., 2005 and Corso et al., 2008).*** Although long-term patency rate is only about 49%, patients in whom stent stenosis occurs do not generally worsen, perhaps because the shunt allows time for collateral circulation to develop ***(Perello et al., 2002).*** The recently introduced, polytetrafluoroethylene-covered stents may improve the patency rates and have been shown to reduce the incidence of TIPS dysfunction in BCS patients ***(Hernandez-Guerra et al., 2004; Cura et al., 2008 and Murad et al., 2008).*** One of the important complications of TIPS procedure is the occurrence of portosystemic encephalopathy ***(Colombato, 2007 and Riggio et al., 2008).***

Hepatic Circulation

The vascular system of solid organs has arterial inflow and venous outflow. The liver is unusual in that it derives inflow from both an arterial and venous source. The hepatic artery (HA) contributes 25% of the liver’s blood supply and 50% of the hepatic parenchyma oxygen supply. The HA is closely related anatomically to the bile ducts and is critical to these structures in that it is the exclusive supplier of blood flow to the biliary system ***(Deshpande et al., 2002).***

The portal vein (PV) contributes the majority of the liver's blood flow (75%) and accounts for the remaining 50% of the oxygen supply. There are no direct vascular connections between the PV and HA circulations. Blood from both systems enters the hepatic sinusoids at different levels and then unites to empty into central veins (CV_s). From the (CV_s), the circulation enters the principal hepatic venous outflow tracts known as the hepatic veins (HV_s). There are three major HV_s (right, middle, and left). Blood leaves the HV to enter the inferior vena cava (IVC) at a level just below the diaphragm before entering the right atrium ***(Gilroy and Sorrell, 2006).***

The liver is divided into eight segments. The segmental division is derived from the vascular supply emanating from the major branches of the left and right portal vein. Accompanying the PV branches to the segments are equivalent first-order divisions of the left and right HAs and bile ducts. The major HVs do not correspond to the segmental division of the liver.

The three HVs, also known as the right, middle, and left HV, lie in the fissures between the hepatic segments ***(Gilroy and Sorrell, 2006).***

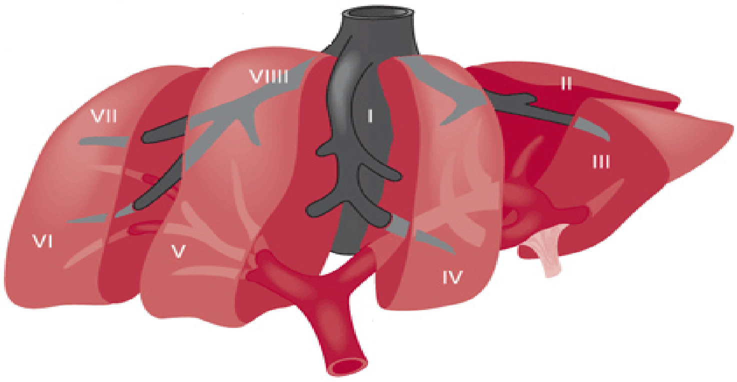

Fig. (1): Segmental anatomy of the liver ***(Feldman, 2010).***

Histologically, ***Rappaport, (1980)*** divided the liver parenchyma into acini incorporating the terminal hepatic arteriole, portal venule, and bile duct with the adjacent liver parenchyma. The terminal vessels of the portal triad form the center of the acinus, and each acinus interdigitates with those adjacent to form the acinar agglomerates.

Physiologically, a gradient of oxygen and nutrient delivery to the surrounding parenchyma is established by the acinar structure. This gradient allows the liver parenchyma, lying between the portal triad and CV, to be separated into zones (Fig 2). Zone 1 contains hepatocytes in close proximity to the sinusoidal inflow and has high oxygen concentrations while zone 3 has lower oxygen tensions and is adjacent to the CV (outflow). These anatomic gradients, by in large, explain the pattern of injury seen in hypoperfusion syndromes where zone 3 hepatocyte injury predominates. With outflow obstruction, hepatocyte loss is also seen in pericentral regions (zone 3); however, in contrast to a hypoperfusion injury, vascular congestion adjacent to the CVs is also present ***(Gilroy and Sorrell, 2006).***

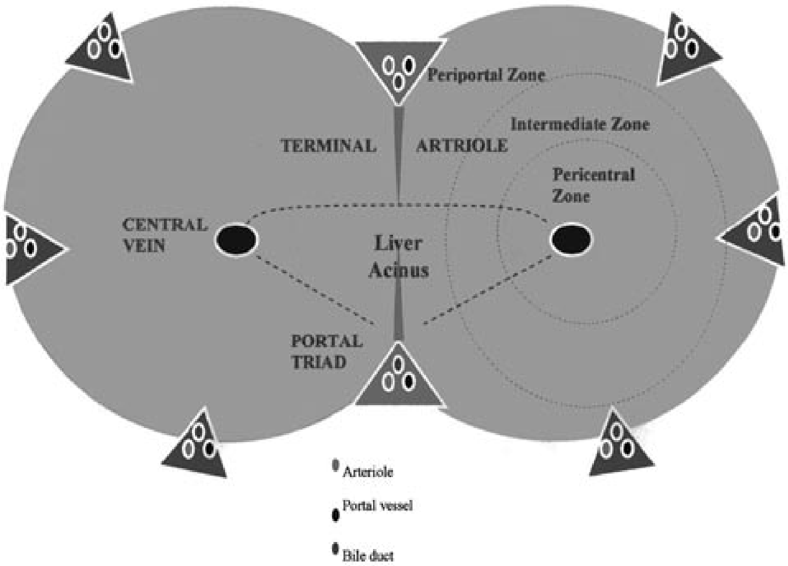

Fig. (2): Zones of the liver parenchyma ***(Gilroy and Sorrell, 2006).***

Anatomy of the hepatic veins:

There are three main hepatic veins. The middle and left veins unite before entering the vena cava in 65% to 85% of individuals ***(Honda et al., 1991).***

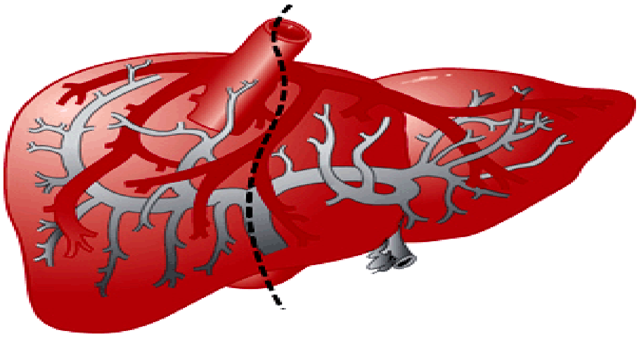

Figure (3): Shows portal, hepatic veins and IVC ***(Jarnagin, 2010).***

In 18% of individuals, there are two right hepatic veins draining into the vena cava ***(Cheng et al., 1997).*** In another 23%, there is a separate middle or inferior right hepatic vein draining segments V or VI, respectively. The veins have variable branching patterns. There are axial veins with four to six orders of branches at acute angles, as well as numerous much smaller branches nearly at right angles ***(Wanless, 2007).***

The caudate lobe and adjacent parenchyma are usually drained by one or two small veins directly into the vena cava caudal to the main hepatic veins. When thrombosis of the main hepatic veins occurs, the veins of the caudate lobe are often spared, allowing survival and compensatory hyperplasia of this lobe ***(Wanless, 2007).***

Anastomoses between branches of the hepatic veins are uncommon in the normal liver but may be more frequent in the presence of diseases with portal hypertension ***(Okuda and Takayasu, 1991).***

Anastomoses between branches of the hepatic veins may become enlarged and may be mistaken for the original hepatic veins on Doppler interrogation. Partial recanalization occurs, often leaving webs in the hepatic veins or vena cava. These webs were formerly thought to be congenital, although most are now considered to be acquired ***(Kage et al., 1992).***

Hepatic Collateral Circulation:

Portal hypertension leads to the development of intra- and extrahepatic venous collaterals ***(Okuda and Matsutani, 1991)*** (**Fig.4).** Extrahepatic collaterals are important, because when dilated to form varices, they are susceptible to rupture and cause massive bleeding. Varices in the submucosa of the gastrointestinal tract are most often a problem, especially in the esophagus and stomach ***(Wanless, 2007).***

Dilated umbilical or paraumbilical veins are found in 11% of patients with cirrhosis **(veins of Sappey)**. They may cause a venous hum and caput medusa at the umbilicus **(Cruveilhier-Baumgarten syndrome).** Their presence implies high pressure in the left PV and, therefore, intrahepatic vascular obstruction. The direction of flow in lower abdominal wall collaterals is caudad if the inferior vena cava is obstructed, as in some patients with Budd-Chiari syndrome ***(Wanless, 2007).***

Varices may be found at sites where the gastrointestinal tract or pancreas becomes retroperitoneal or adherent to the abdominal wall because of pathologic processes. These **“veins of Retzius”** establish connections between the portal bed and the ascending lumbar azygos, renal, and adrenal veins ***(Wanless, 2007)***.

Within cirrhotic parenchyma, shunts are formed by anastomoses between smaller branches of the portal and hepatic veins. These shunts allow blood to bypass the sinusoidal exchange surface, leading to functional impairment. This effect is made worse by the creation of large shunts. In addition, any procedure that decreases portal flow to the sinusoids increases the likelihood of thrombosis, further increasing intrahepatic resistance. Titration of these benefits and liabilities is an important feature of surgical management. Large spontaneous shunts may be beneficial in lowering portal pressure and should not be disturbed without consideration. Portosystemic shunting appears to be responsible for reduced peripheral vascular resistance, possibly through the enhanced release of nitric oxide ***(Bernadich et al., 1997).***

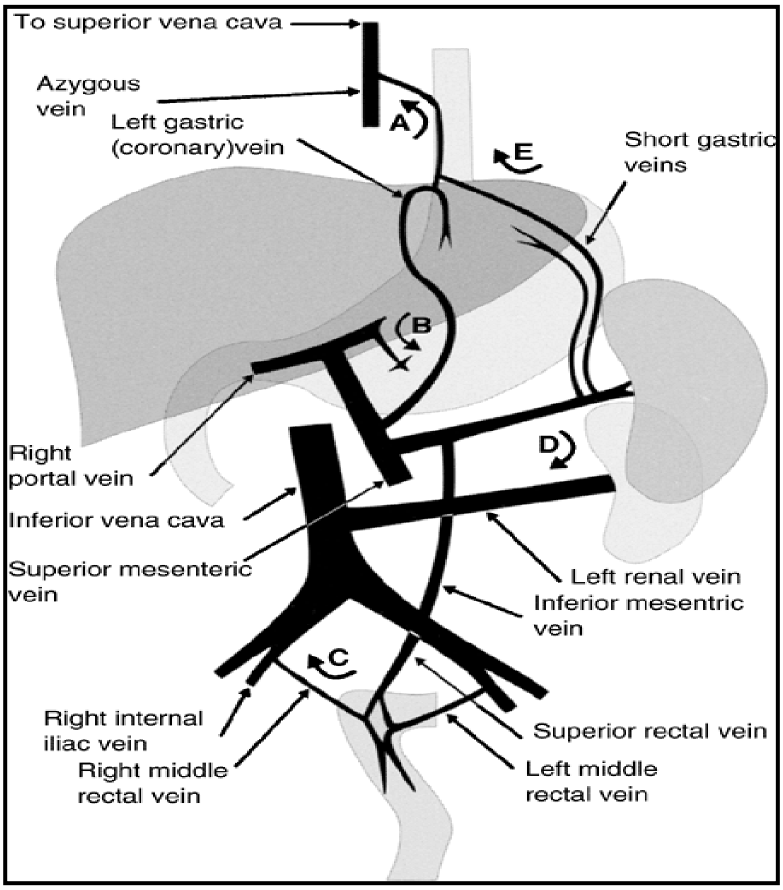

Fig. (4): Diagram of portal circulation ***(Wanless, 1997).***

The most important sites for the potential development of portosystemic collaterals are shown. **A, Esophageal submucosal veins**, supplied by the left gastric vein and draining into the superior vena cava through the azygous vein**. B, Paraumbilical veins,** supplied by the umbilical portion of the left portal vein and draining into abdominal wall veins near the umbilicus. These veins may form a caput medusa at the umbilicus**. C, Rectal submucosal veins,** supplied by the inferior mesenteric vein through the superior rectal vein and draining into the internal iliac veins through the middle rectal veins. **D, Splenorenal shunts:** Created spontaneously or surgically**. E, Short gastric veins** communicate with the esophageal plexus.

Definitions

Budd–Chiari syndrome is defined as hepatic venous outflow obstruction at any level from the small hepatic veins to the junction of the inferior vena cava and the right atrium regardless of the cause of obstruction. Outflow obstruction caused by hepatic veno-occlusive disease and cardiac disorders is excluded from this definition ***(Janssen et al., 2003).***

In 1845, an internist named **George Budd** described the classic triad of abdominal pain, hepatomegaly and ascites. In 1899, pathologist **Hans Chiari** documented the histopathological features of what is now known as the Budd–Chiari syndrome. ***Veno-occlusive disease (VOD),*** also referred to as sinusoidal obstruction syndrome, is ***defined as*** a non-thrombotic obstruction of sinusoids or central hepatic veins due to injury of the sinusoidal wall ***(Deleve et al., 2002).*** Veno-occlusive disease occurs following administration of toxic agents and is, at present, encountered almost exclusively in association with bone marrow transplantation ***(Shulman et al., 1994).***