Non-Invasive Assessment of Fibrosis in Patients with Budd-Chiari Syndrome

Thesis

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وأنزل الله عليك
الكتاب والحكمة
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تَعْلَمُ وكَانَ فَضْلُ
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Introduction

Budd-Chiarisyndrome is an uncommon disorder resulting from an obstructed hepatic venous outflow tract. The obstructive lesion is situated in the main hepatic veins, in the inferior vena cava or in both. The nature, location and extension of the obstruction can be displayed on diagnostic imaging techniques. In addition to this direct evidence, the indirect findings of venous obstruction such as the presence of intra- and extra- hepatic collateral veins, when combined with the altered morphology and enhancement pattern of the liver enables one to arrive at a confident diagnosis ***(Erden, 2007).***

According to the etiology, BCS can be classified as primary (due to intrinsic intraluminal thrombosis or webs) or secondary (due to intraluminal invasion by a parasite or malignant tumor or extraluminal compression by an abscess, cyst or solid tumor)***(Aydinti and Bayraktar, 2007).***

Clinical manifestations of BCS classically include hepatomegaly, right upper quadrant pain, and abdominal ascites. These findings are present in majority of patients***(Darwish et al., 2009).***

According to duration of symptoms and signs of liver disease, BCS can be presented in acute, subacute or chronic form; the most common presentation is the chronic form.A high index of suspicion is necessary for diagnosis because clinical manifestations

and laboratory results are non specific ***(Hoekstra and Janssen,2008).***

Radiological imaging plays an important part in the evaluation of a patient suspected to have BCS. In fact, under current consensus recommendations, radiological imaging is sufficient to make a diagnosis of BCS. The relevant imaging modalities are ultrasonography, computed tomography (CT), magnetic resonance imaging (MRI), nuclear medicine scans, and hepatic venography ***(Kamath, 2006).***

The initial study of choice for documenting hepatic outflow obstruction is Doppler ultrasound with an overall accuracy of approximately 70% ***(Chawla et al., 1999).***

Duplex sonography is a non-invasive method to assess the venous and arterial vasculature. It is easy and fast to perform ***(Gerard-Herman et al., 2006).***

Conventional Doppler sonography yields valuable anatomic and functional information in patients with chronic liver disease & portal hypertension. Color Doppler imaging, by passively superimposing Doppler information on the gray scale image as a color flow map, facilitates detection of vessels that can be missed with gray scale or even conventional Doppler sonography. In addition, color Doppler sonography shows flow direction and flow patterns in real time. This adds physiologic

information without altering haemodynamics by avoiding the injection of contrast material ***(Murakam et al., 2001).***

Non-invasive methods that measure the degree of liver fibrosis have recently been developed, including transient elastography. Hepatic ultrasonic transient elastography (fibroscan) is a new diagnostic method for hepatic fibrosis. It is totally non-invasive and gives an immediate result. Nowadays, fibroscan is a reliable alternative for the non invasive diagnosis of hepatic fibrosis. Several reports have shown that liver stiffness (LS), measured by transient elastography, accurately predicts liver fibrosis in patients with chronic hepatitis C and chronic cholestatic liver diseases ***(Corpechot et al., 2006).***

In a study by ***Foucher, Chanteloup et al. in 2006*** in cirrhotic patients suggested that the higher the value of LS, the higher the risk of liver decompensation. The resistance within the liver, which is an important determinant of portal hypertension (PHT), may be assessed through the measurement of liver stiffness. In keeping with this, ***Kazemi et al. in 2006*** reported that LS accurately predicts the presence of large oesophageal varices.

Aim of the Work

The aim of this work is to evaluate the validity of fibroscan in identifying the degree of fibrosis in Budd Chiari syndrome patients.

Chapter (*I*)
Vascular Anatomy of the Liver

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.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).***

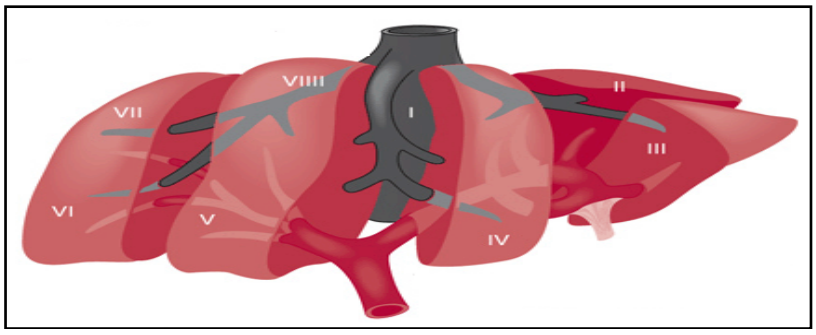

Figure (1): Segmental anatomy of the liver ***(Gilroy and Sorrell, 2006).***

Portal Vein

The portal vein is formed by the confluence of the splenic vein and the superior mesenteric vein. The inferior mesenteric vein usually drains into the splenic vein upstream from the confluence. The main portal vein traverses the porta hepatis before dividing into the left and right portal vein branches. Closer to the liver, the main portal vein typically gives off a short branch (posterior lateral) to the caudate process on the right side***(Abdel-Misih and Bloomston, 2010).***

Anatomy of the hepatic veins:

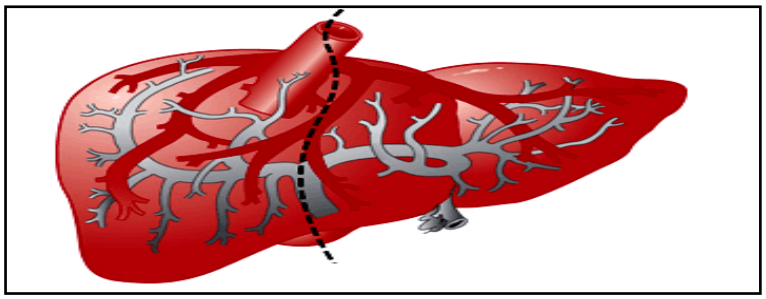

Figure (2): Portal, hepatic veins and IVC ***(Wanless, 2007).***

There are three main hepatic veins. The middle and left veins unite before entering the vena cava in 65% to 85% of individualsIn 18% of individuals, there are two right hepatic veins draining into the vena cava. 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. 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***(Dooley et al., 2011).***

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***(Wanless, 2007).***

There is a large inferior accessory right hepatic vein in 15 to 20% of cases that runs in the hepatocaval ligament. The hepatic vein branches bisect the portal branches inside the liver parenchyma (i.e., the right hepatic vein runs between the right anterior and posterior portal veins; the middle hepatic vein passes between the right anterior and left portal vein; and the

left hepatic vein crosses between the segment III and II branches of the left portal vein ***(Abdel-Misih and Bloomston, 2010).***

Hepatic Collateral Circulation:

Portal hypertension leads to the development of intra- and extrahepatic venous collaterals **(Fig.3).** 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 caudal if the inferior vena cava is obstructed, as in some patients with Budd-Chiari syndrome. 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 **(Wanless, 2007).**

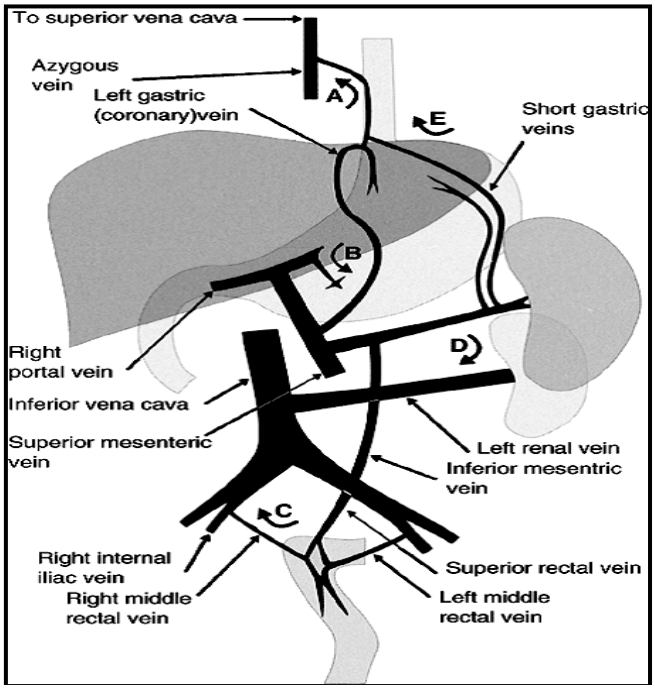

Figure (3): Diagram of portal circulation ***(Wanless, 2007).*** The most important sites for the potential development of portosystemic collaterals are shown. **A, Esophageal submucosal veins**, supplied by the left gastric vein and draining into the superior vena cava through the azygous vein**. B, 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.

Chapter (*II*)
Budd-Chiari Syndrome and Vascular Diseases of the Liver

Vascular Diseases of the Liver

Clinical characteristics of the vascular diseases of the liver are largely dependent on:

1. The nature of the pathologic process (partial or complete obstruction to the outflow or inflow tracts with accompanying inflammation).
2. The extent of hepatic involvement (segmental versus diffuse involvement).
3. The rate of evolution of the pathology.
4. The amount of the accompanying liver parenchymal necrosis.
5. Specific vasculature involvement (HA versus HV)

(Gilroy and Sorrell, 2006).

Insults to the liver's vasculature can be the consequence of a more generalized systemic process (e.g., hypoperfusion during shock or congestion with heart failure) or can result from primary disease processes confined to the liver itself (e.g., Budd-Chiari syndrome) ***(Gilroy and Sorrell, 2006).***

Vascular diseases of the liver

A- Diffuse Involvement

- Hepatic venous outflow obstruction:
  - Budd-Chiari syndrome
  - Veno-occlusive disease (VOD)
  - Congestive hepatopathy.
- Portal vein thrombosis
- Ischemic Hepatitis
- Peliosis hepaticus
- Systemic vascular disease:
  - Polyarteritis nodosa
  - Other vasculitis (SLE)
  - Atherosclerosis
  - Cutaneous bacillary angiomatosis
- Malignancy associated (Hairy cell leukemia)
- Trauma/Iatrogenic

B- Segmental Involvement

- Benign:
  - Hemangioma
  - Osler-weber-rendu
- Malignant vascular neoplasms:
  - Primary (Hemangioendothelioma, Kaposi Sarcoma)
  - Metastatic

(Gilroy and Sorrell, 2006).

Budd – Chiari Syndrome

Budd–Chiari syndrome is a heterogeneous group of disorders characterized by hepatic venous outflow obstruction at the level of the hepatic venules, the large hepatic veins, the inferior vena cava till its junction with the right atrium ***(Valla, 2006).***

Classification:

BCS can be classified according to etiology, site of obstruction, manifestations and duration of the disease***(Janssen et al., 2003).***

BCS is considered primary when obstruction of the hepatic venous outflow tract is the result of an endoluminal venous lesion (thrombosis or web). It is considered secondary when the obstruction results from the presence in the lumen of material not originating from the venous system (malignant tumor or a parasitic mass invading the lumen) or from extrinsic compression by a neighboring tumor (abscesses, cysts, benign or malignant solid tumors)***(Janssen et al., 2003).***

Obstruction of the hepatic venous outflow tract is classified according to its location: small hepatic veins, large hepatic veins, inferior vena cava and combined obstruction of large hepatic veins and inferior vena cava***(Plessier et al., 2008).***

BCS has been recently classified according to site of obstruction into 3 types and 6 subtypes based on lesions in the IVC and/or the HVs: type I, lesions of the IVC including three subtypes: Ia membranous lesion, Ib short segmental occlusion (<5 cm), Ic long segmental occlusion (>5 cm); type II, lesions of the HVs including two subtypes with membranous lesions or diffuse occlusion; type III, mixed type with lesions of the IVC and the HVs***(Zhang and Li, 2007)***.

For descriptive purposes only, the syndrome can be clinically classified as asymptomatic, fulminant, acute, subacute, or chronic ***(Darwish et al., 2009).***

Aetiology

- Haematological:
  1. Polycythaemia vera and other myeloproliferative disorders.
  2. Thrombophilic conditions, eg deficiencies of protein C, protein S, antithrombin III or factor V Leiden.
  3. Antiphospholipid antibody syndrome.
  4. Essential thrombocytosis.
  5. Paroxysmal nocturnal haemoglobinuria.
  - Reduced blood flow: vena caval abnormalities (eg webs, congenital absence of part of the vessel), right heart failure, constrictive pericarditis, right atrial myxoma.
  - Obstetric: the condition can occur during pregnancy and postpartum.