CIRRHOSIS IN ADULTS: OVERVIEW OF DIAGNOSIS AND GENERAL MANAGEMENT

- Cirrhosis represents a late stage of progressive hepatic fibrosis characterized by distortion of the hepatic architecture and the formation of regenerative nodules. It is generally considered to be irreversible in its advanced stages, at which point the only treatment option may be liver transplantation.

Cirrhosis is often suspected in patients with:

- Stigmata of chronic liver disease discovered on physical examination
- Evidence of cirrhosis on laboratory or radiologic testing or by direct visualization while undergoing a surgical procedure
- Evidence of decompensated cirrhosis, which is characterized by the presence of dramatic and life-threatening complications, such as variceal hemorrhage, ascites, spontaneous bacterial peritonitis, or hepatic encephalopathy

-A meta-analysis found that the factors with the best ability to predict cirrhosis in adults with known or suspected liver disease included:

- Presence of ascites (likelihood ratio [LR] 7.2)
- Platelet count <160,000/mm3 (LR 6.3)
- Spider angiomata (LR 4.3)
- Bonacini cirrhosis discriminant score greater than 7 (LR 9.4)

- **Liver biopsy is currently the gold standard for staging hepatic fibrosis**, However, liver biopsy is not necessary if the clinical, laboratory, and radiologic data strongly suggest the presence of cirrhosis and if the results would not alter the patient's management.

liver biopsy has many limitations :

- It is invasive and usually not welcomed by patients.
- It can only sample a small portion of the liver.
- It may be associated with complication (pain, bleeding, bile peritonitis, perforation, transient bacteremia,..).

- These issues have led to the development of noninvasive means to estimate the amount of hepatic fibrosis.

There are several histologic scoring systems for chronic liver disease.

Many use five-point scales such as the METAVIR score:

F0 : No fibrosis

F1: Portal fibrosis without septa

F2: Few septa

F3: Numerous septa without cirrhosis

F4: Cirrhosis

Patients are typically considerd to have significant fibrosis if their score is >=F2

- There are two general categories of noninvasive tests for fibrosis:
  - **Serologic tests.**
  - **Radiologic tests.**
- The specific tests chosen will depend on local availability, but recommendation is for combination use.

IMAGING STUDIES

- Abdominal ultrasound is typically the first radiologic study obtained because it is readily available, provides information about the appearance of the liver and blood flow within the portal circulation, is less expensive than other imaging modalities, and does not expose patients to intravenous contrast or radiation.
- the liver may appear small and nodular. Surface nodularity and increased echogenicity with irregular appearing areas are consistent with cirrhosis, but can also be seen with hepatic steatosis.
- ultrasonography had a sensitivity of 91 percent and a specifity of 94 percent for making the diagnosis

- Computed tomography – CT is not routinely used in the diagnosis and evaluation of cirrhosis. It provides similar information to ultrasonography, but at the expense of radiation and contrast exposure.
- Magnetic resonance imaging : Some authors report that MRI can accurately diagnose cirrhosis and provide correlation with its severity . MRI may also reveal iron overload and provide an estimate of the hepatic iron concentration Magnetic resonance angiography (MRA) is more sensitive than ultrasonography for diagnosing complications of cirrhosis, such as portal vein thrombosis . Unlike CT portal phase imaging, MRA can determine the volume and direction of blood flow in the portal vein.
- Nuclear studies – Radionuclide testing can be useful in suggesting the diagnosis of cirrhosis [65]. 99mTc sulfur colloid is normally taken up by cells of the reticuloendothelial system. In patients with cirrhosis, there may be heterogeneity in the uptake of 99mTc sulfur colloid by the liver a, this test is seldom performed in clinical practice.

SEROLOGIC TESTS

- Serologic markers of hepatic fibrosis can broadly be categorized as indirect or direct:
- **Indirect markers** reflect alterations in hepatic function, but do not directly reflect extracellular matrix metabolism. Examples include the platelet count, coagulation studies,and aminotransferases.
- **Direct markers of fibrosis** reflect extracellular matrix turnover. Examples include procollagen types I and III, hyaluronic acid, and tissue inhibitor of metalloproteinase

CLINICAL USES

- Primarily used for staging of fibrosis in patients with chronic liver disease.(differentiate significant fibrosis F2-F4 from those with minimal or no fibrosis F0-F1)
- Useful to determine if there is progression of fibrosis.
- May also have a role in monitoring patients taking medications associated with chronic liver damage, such as methotrexate.

INDIRECT MARKERS OF FIBROSIS

AST to platelet ratio index

- The APRI is based on the AST level and platelet count and is easy to calculate. The APRI is calculated using the AST elevation (which is the AST level divided by the upper limit of normal [ULN] for the lab) and the platelet count per mm3 divided by 1000.

APRI = (AST elevation/platelet count) x 100

- As an example, a patient with an AST level of 90 international unit/L in a lab with an ULN = 45 international unit/L and a platelet count of 120,000/mm3 would have an APRI of:

(2/120) x 100 = 1.67

- FibroTest, FibroSure, and ActiTest
- Hepascore
- AST/ALT ratio
- Other indirect markers:

  fib-4 index, **nafld fibrosis score**, pga index, fibroindex, forns index, fibrometer, brad score,

ELASTOGRAPHY

- **Ultrasound-based elastography:** - shear wave elastography:

  - transient Strain elastography

  -point-SWE

Ultrasound-based transient elastography is the most studied radiologic method for staging hepatic fibrosis, When is used in a clinical setting**, commonly cutoffs for significant fibrosis and cirrhosis are >7 kPa and >11 to 14 kPa, respectively.**

- **Magnetic resonance elastography:**

MRE has the advantage of scanning the entirel liver and dosnot depend on an acustic window. It may also detect lesions within the liver.

- Using multiple serologic panels or combining serologic panels with radiographic imaging may improve the ability to correctly assess the degree of a patient's fibrosis.

GENERAL MANAGEMENT

-Slowing or reversing the progression of liver disease

- Preventing superimposed insults to the liver

- Identifying medications that require dose adjustments or should be avoided entirely

-Managing symptoms and laboratory abnormalities

- Preventing, identifying, and treating the complications of cirrhosis

- Determining the appropriateness and optimal timing for liver transplantation

Preventing superimposed insults to the liver

- Vaccinations
- Avoidance of hepatotoxins
- Medication adjustments

Management of symptoms and laboratory abnormalities

- Muscle cramps
- Umbilical hernias
- Hyponatremia
- Thrombocytopenia or elevated INR

PREVENTING AND IDENTIFYING COMPLICATIONS

- **Variceal bleeding:**
- **Hepatocellular carcinoma**
- **Spontaneous bacterial peritonitis**
- **Hepatic encephalopathy**
- **Portal vein thrombosis**
- **Hepatorenal syndrome**
- **Secondary infections**

LIVER TRANSPLANTATION

- Liver transplantation is the definitive treatment for patients with decompensated cirrhosis.
- It is important to determine whether patients may be eligible for transplantation and to refer them to a transplant center for evaluation.
- Several guidelines are available which help determine when referral for liver transplantation may be beneficial.
- The decision to proceed to liver transplantation (either cadaveric or live donor) depends upon the severity of disease, quality of life, and the absence of contraindications