Budd–Chiari Syndrome (BCS)

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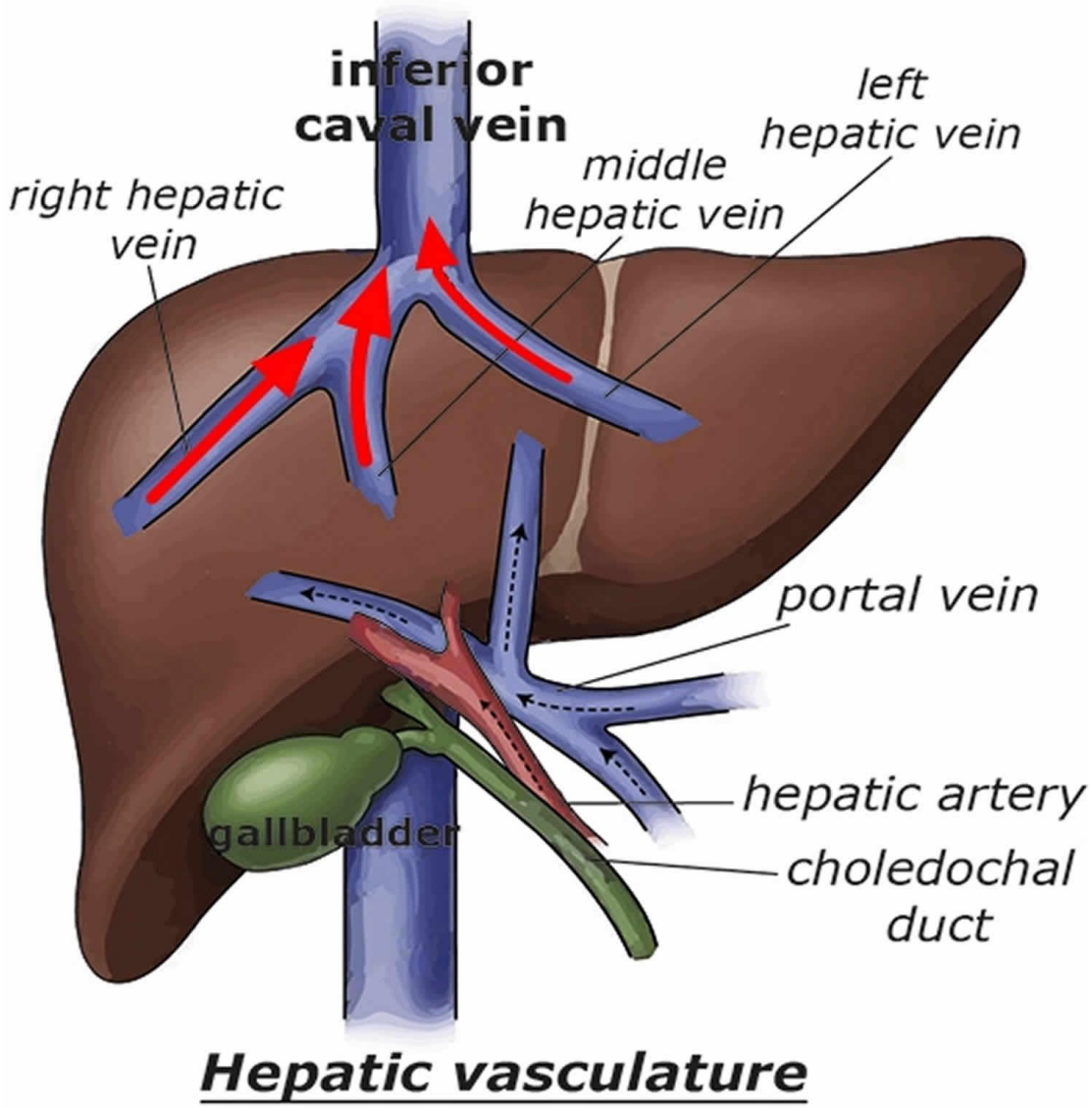
GILDRC, IUMS

Budd–Chiari Syndrome (BCS)

- An obstruction of hepatic venous outflow, at the level of the hepatic veins and/or (IVC), in the absence of right-sided heart failure, CP, or sinusoidal obstruction syndrome.

- • The obstruction may

.....be primary or secondary ,



clinical spectrum

- The ranges from acute fulminant disease with painful hepatomegaly, ascites, and liver failure, to chronic forms with progressive portal hypertension, variceal bleeding, and cirrhosis.

- Clinical Features
- Classical triad: Ascites, hepatomegaly, abdominal pain (seen in ~2/3 of cases).
- Other signs: jaundice, splenomegaly, variceal bleeding.

Form / Stage	Onset	Clinical Features	Lab Findings	Imaging	Intervention
Acute BCS	Days to weeks	- Right upper quadrant pain- Rapid ascites- Tender hepatomegaly	- Elevated AST/ALT- Mild-moderate bilirubin rise- INR may be prolonged	- Thrombosed hepatic veins- Hepatomegaly	- Urgent anticoagulation- Consider TIPS if no improvement- Supportive care
Subacute BCS	Weeks to a few month	- Moderate ascites- Hepatomegaly, mild pain- Mild jaundice	- Elevated liver enzymes- Mild synthetic dysfunction	- Partial obstruction- Collateral formation	- Anticoagulation- Evaluate for angioplasty/ stenting or TIPS if needed
Chronic BCS	Months to years	- Signs of portal hypertension (splenomegaly, varices, refractory ascites)- Fatigue, mild hepatomegaly	- Mild enzyme elevation- Variable synthetic dysfunction	- Thrombosed veins- Collaterals, caudate lobe hypertrophy	- Anticoagulation- Angioplasty/stenting- TIPS if ascites/complications- Liver transplant in severe cases
Fulminant BCS	Days	- Severe jaundice- Hepatic encephalopathy- Rapid liver failure	- Marked bilirubin elevation- Coagulopathy	- Extensive hepatic vein/ IVC thrombosis	- Emergency TIPS or liver transplant- Intensive supportive care

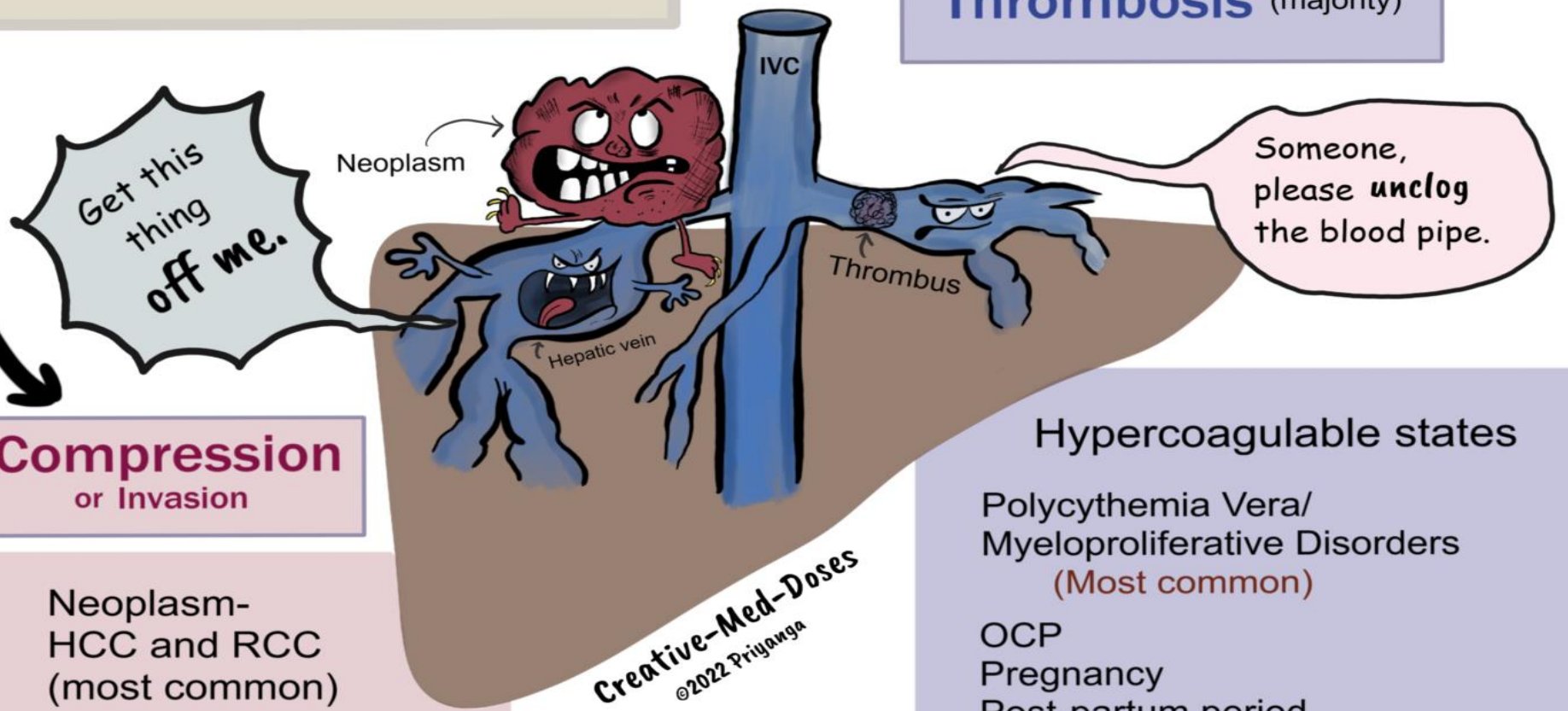
Epidemiology & Etiology

- Rare, incidence 1–2 per million/year.
- Strongly associated with prothrombotic states:
- Myeloproliferative neoplasms (esp. JAK2 V617F mutation).
- Antiphospholipid syndrome, factor V Leiden, protein C/S deficiency.
- In Asia: membranous IVC webs/stenosis are common causes.
- …..

Budd-Chiari Syndrome: Etiology

Hepatic vein obstruction

Thrombosis (majority)



Compression or Invasion

Neoplasm-
HCC and RCC
(most common)

Space Occupying lesions–
Hepatic cyst, aspergillosis

Hypercoagulable states

Polycythemia Vera/
Myeloproliferative Disorders
(Most common)

OCP
Pregnancy
Post-partum period

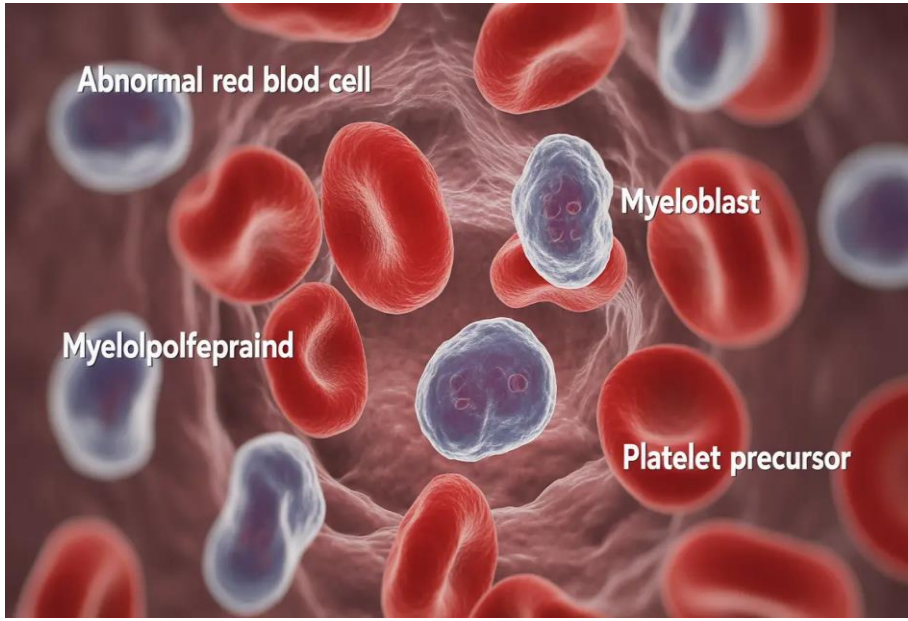
Antiphospholipid antibody syndrome

Paroxysmal Nocturnal hemoglobinuria (PNH)

Clotting abnormalities

Causes of BCS

- 1. Myeloproliferative Neoplasms (MPNs) – The Most Common Cause
- responsible for over 80% of BCS cases.
- JAK2 V617F Mutation: most important cause40-50% of all BCS patients.
- Testing for this mutation is mandatory in every case.
- · Calreticulin (CALR) Mutation: in approximately 3-7% of BCS cases.
- · MPL Mutation: Found in about 1-5% of cases.
- · "Triple-Negative" MPNs: Patients negative for JAK2, CALR, and MPL occult MPN diagnosable by bone marrow biopsy,



2. Other Systemic Hypercoagulable States

- Paroxysmal Nocturnal Hemoglobinuria (PNH): A rare acquired disorder where RBCs are susceptible to complement-mediated destruction, leading to a high risk of thrombosis. Diagnosed by flow cytometry (CD55, CD59).
- Antiphospholipid Syndrome (APS): An autoimmune disorder characterized by antibodies that cause arterial and venous thrombosis.
- Inherited Thrombophilias: Often act as co-factors in a "multiple-hit" scenario.
- Factor V Leiden mutation
- Prothrombin G20210A mutation
- Deficiencies of Protein C, Protein S, or Antithrombin III

The "Multiple-Hit" Hypothesis

- A cornerstone of the modern understanding. EASL emphasizes that BCS typically requires more than one prothrombotic risk factor to manifest.
-
- · Example : A patient with an underlying JAK2+ MPN (first hit) who starts taking oral contraceptive pills (second hit).

3. Local Risk Factors & Miscellaneous Causes

- These are less common but must be considered, especially if hematological workup is negative.
-
- Abdominal Malignancies: Tumors causing compression or invasion of the hepatic veins or IVC (e.g., HCC,RCC).
- Inflammatory Disorders: Behçet's disease, IBD, sarcoidosis.
- Infections: Liver abscess, hydatid cyst, aspergillosis.
- Trauma or Iatrogenic injury (e.g., after liver surgery).
- Membranous Obstruction of the IVC: A common cause in certain parts of the world (e.g., South Africa, Asia), often linked to poor socioeconomic conditions and recurrent infections.

4. Idiopathic

- This is a diagnosis of exclusion. With modern diagnostic techniques, <10% of cases remain truly idiopathic after a complete workup. EASL stresses that a "full screening must be performed" before this label is applied.
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Category Specific Causes Key Diagnostic Tests

- 1. Systematic Screening: A full etiological workup is mandatory for every BCS patient.
- 2. Test for MPNs First: Begin with JAK2 V617F, then CALR and MPL mutations. Even if negative, a BMB should be considered if clinical suspicion is high.
- 3. Look for Multiple Hits: Finding one cause (e.g., Factor V Leiden) should not stop the investigation; continue searching for a concomitant MPN or other factor.
- 4. PNH is a Must-Rule-Out: Flow cytometry for PNH is a standard part of the diagnostic algorithm.
- In conclusion, according to EASL, BCS is primarily a hematological disorder manifesting in the liver.

High clinical suspicion in patients with unexplained ascites + hepatomegaly + abdominal pain.

- First-line imaging:
  - Doppler Ultrasound: sensitivity 85–90%, non-invasive, first choice.
  - CT or MRI (with venography): confirmatory, assess extent, chronic vs acute, and plan intervention.
- Key findings:
  - Non-visualization or thrombosis of hepatic veins/IVC.
  - Collateral “spider-web” veins, intrahepatic collateral vessels ("comma sign"),
  - Caudate lobe hypertrophy (drains directly into IVC), splenomegaly, ascites,
  - Heterogeneous liver enhancement.

Multi-Phase Contrast-Enhanced CT (Computed Tomography) Angiography

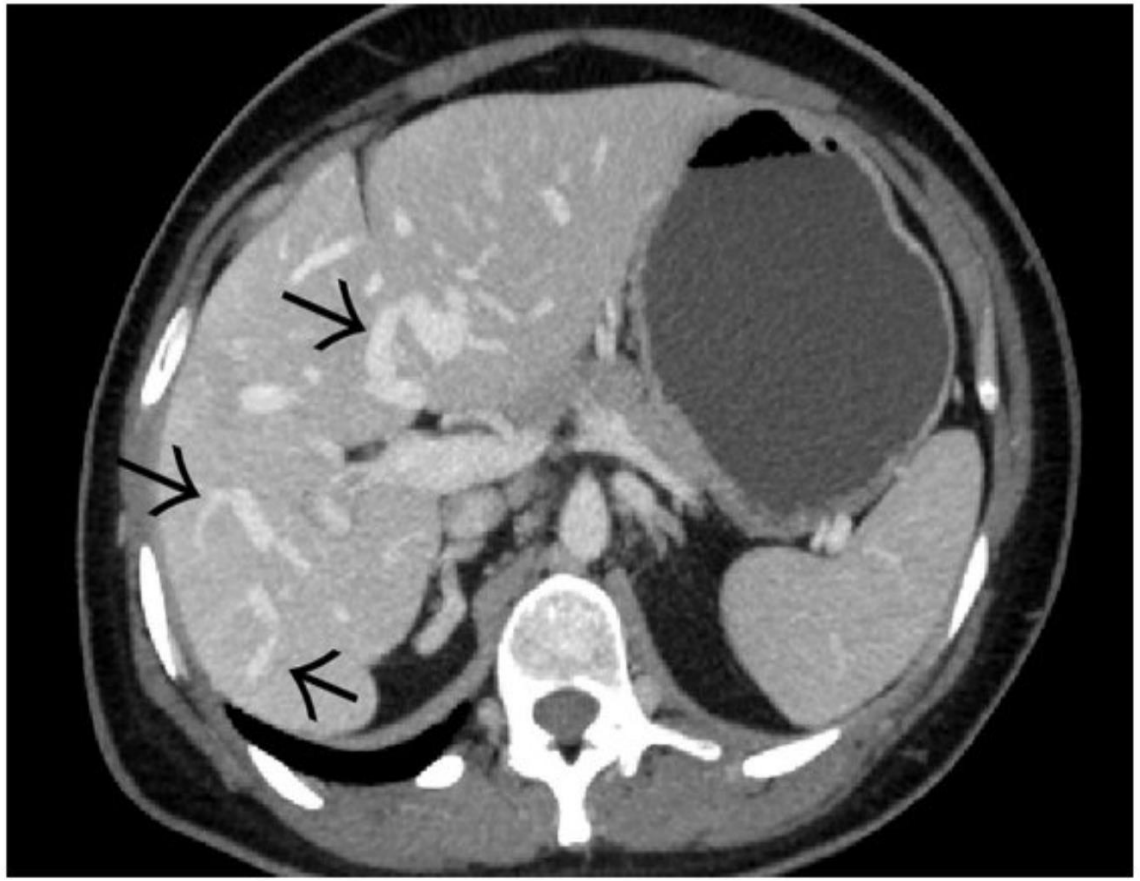
- First-line diagnostic and pre-procedural planning tool. Provides a comprehensive overview.
- · Key Findings:
- · Acute: Non-opacification of HVs/IVC, peripheral liver hypoattenuation with central enhancement ("flip-flop" sign), heterogeneous "nutmeg" liver enhancement.
- · Chronic: HV occlusion, caudate lobe hypertrophy, large regenerative nodules, collateral veins.
- · Excellent for ruling out other causes of abdominal pain and liver dysfunction.

Multi-Phase Contrast-Enhanced MRI (Magnetic Resonance Imaging) with MR Venography

- First-line alternative to CT, superior for characterizing parenchymal changes and benign regenerative nodules. Ideal for patients where radiation exposure is a concern (e.g., young patients).
- ·Key Findings:
- Similar findings to CT but with superior soft-tissue contrast.
- Thrombus appears as lack of flow void or filling defect on contrast-enhanced sequences.
- · T2-weighted images: Can show parenchymal

  edema in acute stages.
- · MR Elastography: Can be added to assess liver

  stiffness for risk stratification and prognosis.



Axial CECT images from four different patients demonstrating comma-shaped intrahepatic collaterals (arrows) demonstrating varying degrees of patency.

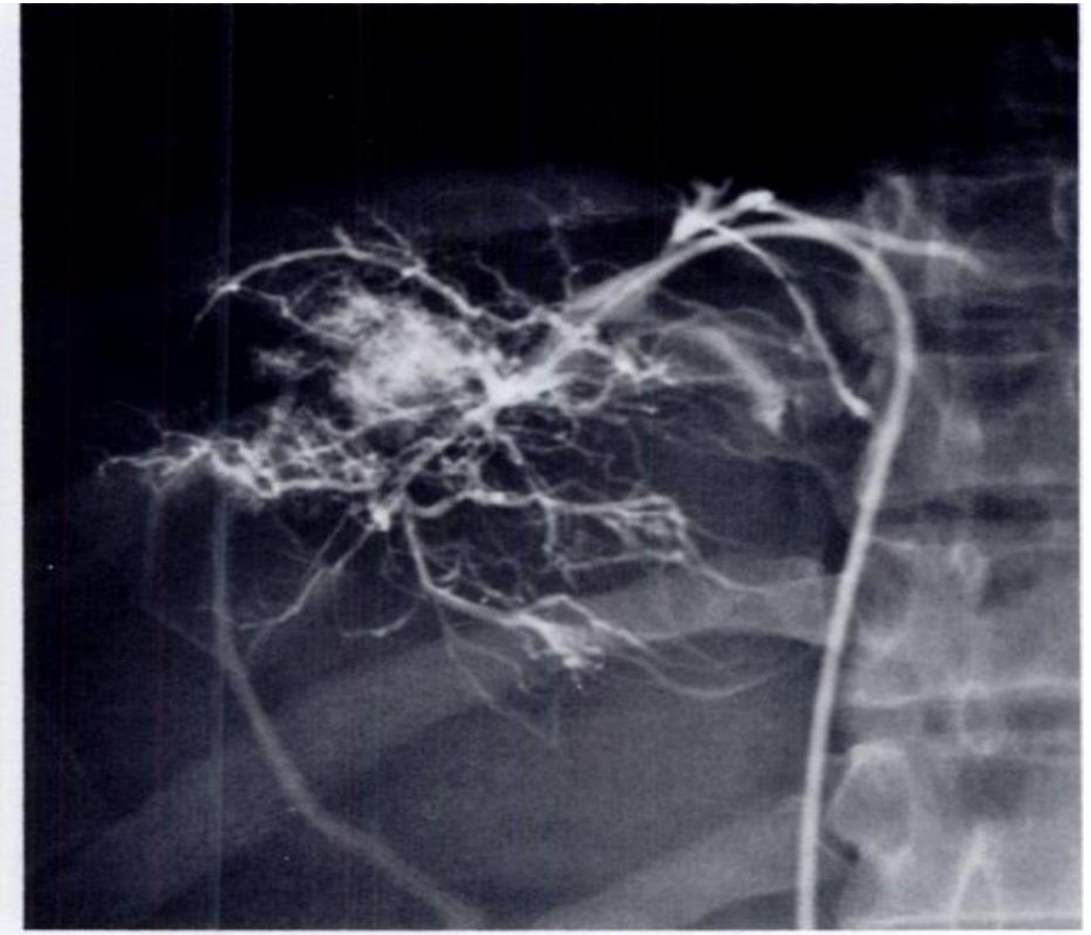


Fig. 4.—Selective hepatic wedge venogram shows characteristic "spider-web" pattern of collateral intrahepatic veins.

4. Hepatic Venography (Invasive)

- Role: No longer a primary diagnostic tool.

- Reserved for when non-invasive imaging is inconclusive or, more commonly, as the first part of a planned therapeutic intervention (e.g., angioplasty, stenting, TIPS).
- Procedure: Involves injecting contrast directly into the venous system via a catheter to map out the blockages.

Summary of the EASL 2024 Imaging Approach

- Doppler US is the best initial test.
- Contrast-enhanced CT or MRI is required to confirm the diagnosis, define the anatomy and extent of thrombosis, and rule out mimickers.
- The choice between CT and MRI depends on local expertise, availability, and patient factors.
- The imaging findings are always interpreted in conjunction with the clinical presentation and hematological workup (e.g., JAK2 mutation testing).
- The shift is towards non-invasive diagnostics, with invasive venography being primarily therapeutic.

- Refinement of diagnostic and risk-stratification tools is a cornerstone of the modern management of Budd-Chiari Syndrome (BCS). It allows for a more personalized and proactive treatment approach.

- The goal is no longer just to diagnose BCS, but to quickly assess the severity of liver injury, predict the patient's clinical course, and guide the most appropriate treatment step.

- →identify high-risk patients early and escalate therapy before irreversible liver damage occurs, which is the key reason survival rates have soared above 85-90%

Refined Diagnostic and Risk-Stratification Tools in BCS

1-(VCTE / FibroScan®)

- ➢ In BCS, stiffness reflects both fibrosis and acute congestion from the outflow obstruction.
- ✓ strongly predicts outcomes and helps choose the right therapy.
- Provides a quantitative threshold for escalating care.
- LSM < 25 kPa: Suggests early disease or good potential for recovery with medical therapy alone.
  LSM between 25 - 50 kPa: Indicates significant congestion/fibrosis. This group has a high likelihood of needing an invasive procedure like TIPS and should be referred for early radiological intervention.
- · LSM > 50 kPa: Signifies severe, likely irreversible liver damage. may not improve with TIPS alone and should be promptly referred for liver transplant evaluation.
- · Monitoring Tool: LSM can be used serially to track response to treatment (e.g., a decreasing LSM after TIPS indicates successful decompression).

2. Advanced Cross-Sectional Imaging

Modern CT and MRI are diagnostic powerhouses that provide a comprehensive map.

- Multiphase CT Angiography & MR Angiography:
- · Diagnosis: Clearly identifies the level and extent of obstruction (hepatic veins, IVC, or both).
- · Parenchymal Assessment: Shows characteristic signs of outflow obstruction:
- · Pre-procedural Planning: Provides an essential "roadmap" for the interventional radiologist planning an angioplasty, stenting, or TIPS procedure by showing vessel patency and anatomy.

- · MR Elastography: An alternative to FibroScan that can provide a more precise map of stiffness across the entire liver, though it is less readily available.

3. Prognostic Scoring Systems

These scores help objectify the severity of illness and guide the urgency of intervention.such as:Liver function test,Model for End-Stage Liver Disease (MELD) Score:

- 4. Sophisticated Hematological Workup

Step-wise Management of BCS (EASL 2024)

➢ Step 1 – Medical Therapy

- •Immediate anticoagulation
- •Treat underlying disease.
- •Goal: prevent thrombus progression + treat root cause.

➢ Step 2 – Radiological Recanalization

•Preferred if feasible: balloon angioplasty ± stent, especially for short segment hepatic vein or IVC obstruction.

➢ Step 3 – TIPS (Transjugular Intrahepatic Portosystemic Shunt)

- •Standard of care if recanalization is not possible or ineffective.
- •Goal: decompression of congested liver, control ascites, relieve portalHTN ,

➢ Step 4 – Liver Transplantation

•Indication: liver failure, progressive disease, or TIPS failure.

Step 1: Immediate Anticoagulation & Specific Disease-Modifying Therapy.

➢ The goals of this step are:

✓ Prevent Clot Extension: Stop the existing thrombus from growing larger.

✓ Prevent New Clots: Mitigate the extreme risk of thrombosis in other vascular beds.

✓ Treat the Root Cause: Address the underlying driver of the hypercoagulable state, not just its symptom (the liver clot).

Immediate Anticoagulation

Rathional: the clot can propagate, worsening liver congestion and leading to complete occlusion. Furthermore, patients with BCS are at a high risk of thrombosis in other vascular beds ,

- · First-Line Agent: Low Molecular Weight Heparin (LMWH)
- · Examples: Enoxaparin, Dalteparin.

Transition to Long-Term Oral Anticoagulation:

➢Vitamin K Antagonists (VKAs like Warfarin) :

- Cornerstone of long-term anticoagulation in BCS for decades.
- Effectivein preventing recurrence is well-documented. careful INR monitoring (target INR 2-3).
- Drawbacks:

✓Require frequent blood tests (INR monitoring) to ensure the dose ,

✓their effect is influenced by diet and other medications.

Important Exception – (APS): For patients with APS, is strongly preferred over DOACs … … … … superior efficacy in preventing recurrent thrombosis in this specific population.

➢The Emerging Concept: Direct Oral Anticoagulants (DOACs)

- Drugs like Rivaroxaban, Apixaban, and Edoxaban :

✓inhibit specific clotting factors (Xa or IIa),

✓taken at a fixed dose and do not require routine monitoring

- Lack of RCTs: There are no large randomized controlled trials comparing DOACs to warfarin specifically in BCS patients.

✓Several large registry studies and cohort analyses :DOACs are non-inferior to warfarin in preventing recurrent thrombotic events in BCS.

- Potential Safety Benefit:

✓Have a lower risk of major bleeding complications, particularly intracranial hemorrhage.

- Current Recommendations and Considerations:
- Off-Label Use: Using DOACs for BCS is still considered "off-label," but it is becoming increasingly common in clinical practice based on the accumulating evidence.

Important Exceptions:

1-Antiphospholipid Syndrome (APS)

- ✓ not recommended for APS patients

2-Severe Liver Impairment:

- ✓ Not advised in patients with very advanced cirrhosis (Child-Pugh B or C) due to unpredictable drug levels and increased bleeding risk. In these cases, warfarin or LMWH are preferred.
- ✓ Shared Decision-Making: The choice between warfarin and a DOAC is made on a case-by-case basis, weighing the convenience and potential safety of DOACs against the longer track record of warfarin, especially for patients with specific conditions like APS.

Specific Disease-Modifying Therapy

- >80% of patients have an underlying MPN, simply anticoagulating is insufficient. You must target the bone marrow disorder itself.

✓ First-Line Cytoreductive Options (Started concurrently with anticoagulation):

- · Hydroxyurea (Hydroxycarbamide):
- Pegylated Interferon-alpha (IFN-α):

✓· Second-Line / Targeted Therapy:

- · Ruxolitinib (a JAK1/JAK2 inhibitor)
- …….

Restoring Hepatic Outflow: Minimally Invasive Procedures

- The primary goal of these procedures →decompress the congested liver by creating a new pathway for blood to flow out.
- Through endovascular (within the blood vessels) techniques, which are highly effective and avoid the need for major surgery.
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- The two main procedures :Angioplasty/Stenting and TIPS (Transjugular Intrahepatic Portosystemic Shunt). The choice between them depends on the pattern and extent of venous blockage.

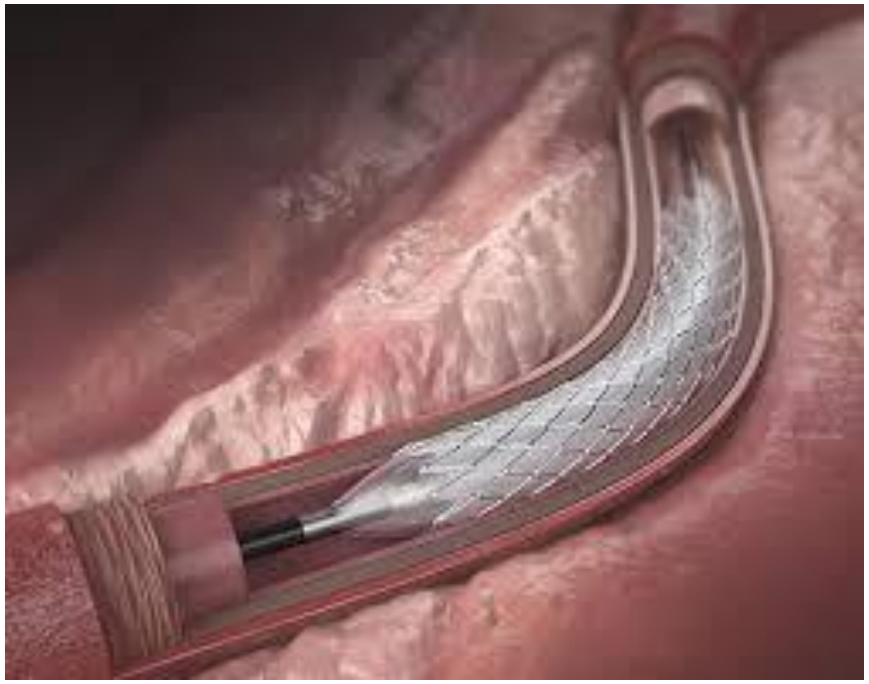
1. Hepatic Vein Angioplasty and Stenting

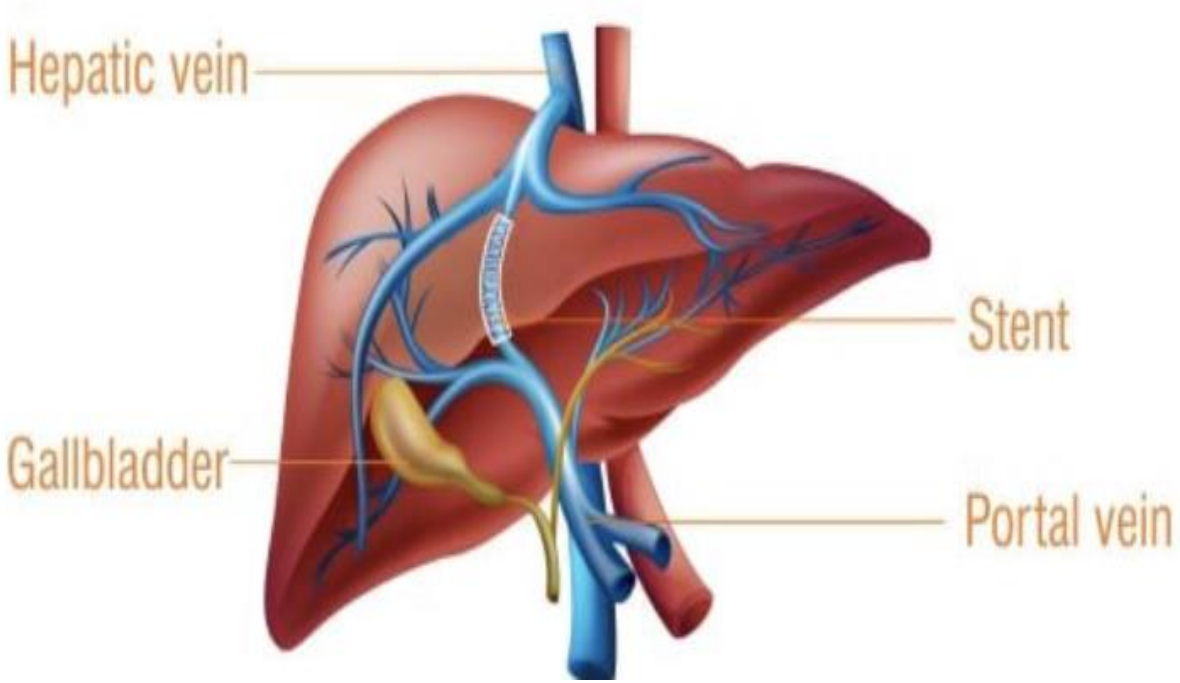
- This is the first-line interventional option when technically feasible.
- Ideal Candidate: Patients with a short-segment stenosis (narrowing) or occlusion (blockage) in one or more hepatic veins or the inferior vena cava (IVC), with well-preserved liver function.
- Balloon Angioplasty: Stent Placement: A metal mesh stent , PTFE(Polytetrafluoroethylene)-covered stents are preferred to prevent restenosis (re-narrowing) from tissue in-growth.

- · Advantages:
- · Physiological: Restores the normal outflow pathway.
- · Minimally Invasive: Low complication rate.
- · Preserves Liver Function: Does not divert nutrient-rich blood from the liver.
- · Outcome: Technical success is high (>90%), and it can be curative for focal lesions.

2. Transjugular Intrahepatic Portosystemic Shunt (TIPS)

- ➢the most revolutionary procedure for BCS.
- ✓Rescue to Preemptive TIPS





➢ Ideal Candidate:

- ✓ Patients with diffuse obstruction of all hepatic veins.(the obstruction : not just stenosis
- ✓ but extensive thrombosis, multiple hepatic veins blocked, or unsuitable lesion for stent).
- ✓ Those with refractory ascites or worsening liver function despite medical therapy.
- ✓ Liver failure progression / decompensation ,If signs of hepatic decompensation (worsening bilirubin, synthetic dysfunction…) become severe and early steps fail,
- ✓ As a bridge to liver transplantation.

➢Stent Placement:

✓A PTFE-covered stent graft is deployed in this tract to keep it open, forming the "shunt." This shunt bypasses the blocked hepatic veins entirely, allowing blood to flow directly from the portal system to the systemic circulation.

Primary Patency Rates of covered stents at 1 year exceed 80-90%, compared to <50% for bare stents.

✓Pressure Measurement: The pressure gradient between the portal vein and systemic vein is measured before and after.

✓The goal is to reduce this gradient to <12 mmHg, effectively decompressing the liver.

Portosystemic Pressure Gradient (PSG) Monitoring

- Portosystemic Pressure Gradient (PSG)—the difference in pressure between the portal vein and the (IVC).

- · The Goldilocks Principle:
- · Too High (PSG >12 mmHg): The TIPS is not functioning effectively. Ascites and varices may persist.
- · Just Right (PSG 8-12 mmHg): Adequate decompression of the liver is achieved,
- · Too Low (PSG <8 mmHg): Excessive shunting of blood flow away from the liver occurs. increases the risk of (HE) and lead to liver failure

➢ Advantages:

- Highly Effective: Rapidly resolves ascites and improves liver function.
- Life-Saving: Can rescue patients from acute liver failure.
- Definitive Treatment: For many patients, a successful TIPS eliminates the need for transplantation.

➢Risks & Management:

✓ Hepatic Encephalopathy (HE): The most common complication,

usually manageable with diet and

medications like Lactulose and Rifaximin.

✓ Shunt Dysfunction: Regular ultrasound surveillance is required.

Covered stents have significantly

reduced this risk.

Outcome: TIPS has transformed prognosis, with 5-year survival rates now exceeding 80-85% in BCS patients.

The modern approach is a structured escalation:

- 1. Start: If a patient has a short-segment blockage, attempt angioplasty/stenting first.
- 2. Escalate: If stenting is not possible, fails, or if the patient presents with severe disease (high MELD score, refractory ascites), proceed directly to TIPS.
- 3. Rescue: If TIPS fails or the liver continues to deteriorate, the final step is liver transplantation.

Liver Transplantation in BCS: The Final Option

- Reserved for specific, well-defined scenarios where all other treatments have failed to halt the progression of liver damage.
-

➢Timing: not taken lightly. It is reserved for two broad categories:

✓A. Acute Liver Failure (Fulminant Presentation)

· These patients are often too sick for TIPS or have anatomy that makes TIPS impossible. They require urgent transplantation as a life-saving measure.

✓ B. End-Stage Liver Disease Despite Maximum Medical & Interventional Therapy: This is the more common scenario.

Reserve Transplant for Failures:as a salvage therapy or safety net for patients whose disease progresses despite receiving all other appropriate treatments.

- Failure of Medical Therapy: Their condition deteriorates (increasing ascites, worsening liver function tests) even on optimal anticoagulation and treatment of the underlying blood disorder (e.g., MPN).
- Failure of Radiological Intervention:

Technical Failure: The anatomy makes it impossible to perform a TIPS or angioplasty/stent.

- Clinical Failure: The patient does not improve after a technically successful TIPS/stent, or the TIPS/stent fails repeatedly (e.g., clots off) despite medical management.
- Development of Irreversible Complications: The patient progresses to decompensated cirrhosis with complications that cannot be controlled (e.g., recurrent hepatic encephalopathy, hepatorenal syndrome) or develops acute liver failure.
- Development of Hepatocellular Carcinoma (HCC)

Outcomes: Success and Long-Term Management

Excellent Survival:

- Outcomes : very good, with 5-year patient survival rates exceeding 80% and often reaching 90% in experienced centers.
- → transplantation completely corrects the underlying mechanical problem of hepatic outflow obstruction.

After LT:

- **Preventing Recurrence**: The key to long-term success is preventing BCS from recurring in the new liver. This requires:

✓ **Lifelong Anticoagulation**: To manage the persistent systemic hypercoagulable state.

✓ **Lifelong Management of the Underlying Disorder**: Continued treatment for the MPN (e.g., with hydroxyurea) or PNH (e.g., with eculizumab) is absolutely essential.

✓ **Other Long-Term Management**: Like all transplant recipients, patients require lifelong immunosuppression to prevent organ rejection and are monitored for related side effects (infections, kidney toxicity, metabolic disorders, and malignancy risk).

Long-Term Monitoring in Budd–Chiari Syndrome

1. Hepatocellular Carcinoma (HCC) Surveillance,

2. Prognostic Modeling (Risk Stratification)

The goal: predict who will do well on anticoagulation alone vs who needs earlier intervention (TIPS/LT).

Prognostic Modeling (Risk Stratification)

- a) Clinical + Biochemical Parameters
  - Bilirubin, INR, Albumin
  - MELD score or Child–Pugh often used.
  - Persistent elevation (or rising trend)

- b) Dynamic Monitoring
  - Symptom trajectory matters:
  - If ascites, pain, or hepatomegaly improve → good sign.
  - If not improving within 1–2 weeks on anticoagulation → escalate therapy

- c) Imaging + Function Combined

- d) Emerging Scores
  - Some centers use BCS-TIPS prognostic scores (combining bilirubin, INR, creatinine, encephalopathy, age) to predict survival after TIPS.
  - These models are still being refined, but the concept is personalized thresholds for escalation.

Follow-up & Escalation Plan

Timeline	Assessments	Escalation Criteria
1 Month	Clinical review, LFT/INR, Creatinine, Doppler US, Baseline FibroScan	No improvement or worsening → Step 2
3 Months	Labs, Doppler US, Elastography (if available)	Signs of deterioration → Step 2
6 Months	Clinical review, Labs, Doppler US, ± MRI	Signs of deterioration → Step 2
12 Months	Full reassessment: Labs, Doppler, FibroScan, ± MR elastography	Signs of decompensation → Step 2/3
Yearly	Repeat annual follow-up as above	Persistent/worsening dysfunction → Consider transplant

TAKE-HOME MESSAGE

- Early diagnosis is crucial – use Doppler US, CT, or MRI
- Immediate Anticoagulation & Specific Disease-Modifying Therapy.
- Step-wise management is recommended: medical therapy → angioplasty/stenting → TIPS → liver transplantation.
- Early escalation (not passive waiting) improves survival; lack of improvement within days–weeks signals need for intervention.
- Non-invasive tools (Doppler, FibroScan, MRI) …. increasingly integrated for monitoring and prognosis.
- Multidisciplinary follow-up is essential, as long-term outcomes depend on timely shunt surveillance and transplant evaluation when needed.


Thank
You