Vascular disorders of the liver– Full Clinical Guideline

Reference no:CG-T/2013/223

Collectively includes a number of conditions, including Budd-Chiari syndrome (BCS) and portal vein thrombosis (PVT) that can cause non-cirrhotic portal hypertension with ensuing complications. Aetiological factors can be local or systemic.

	BCS	PVT
Risk factor	Frequency (%)	Frequency (%)
Thrombophilia		
Inherited	21	35
Acquired	44	19
Myeloproliferative neoplasm	49	21
JAK2 pos	29	16
Hormonal factors	38	44
Oral contraceptives	33	44
Pregnancy	6	0
PNH	19	0
Other systemic factors	23	n.d.
Local factors	0	21

BCS, Budd-Chiari syndrome; PVT, portal vein thrombosis; PNH, paroxysmal nocturnal haemoglobinuria; n.d, no date.

En-Vie study of patients with BCS (n=163) and PVT (n=105). Prothrombotic factors in 84% of BCS and 42% of PVT.

Note JAK-2 mutation present in nearly all patients with polycythaemia rubra vera and 50% of those with essential thrombocythaemia and primary myelofibrosis.

Budd–Chiari Syndrome (BCS) - hepatic venous outflow obstruction

The level of obstruction can be located from the small hepatic venules up to the entrance of the IVC into the right atrium.

Presentation: ranges from asymptomatic to fulminant acute liver failure

- Classic symptoms - fever, abdominal pain (61%), hepatomegaly (67%) and ascites (83%) +/- lower extremity oedema, GI bleeding (5%) and encephalopathy
- 15% have co-existent PVT
- 60-80% of patients may have hepatic nodules on imaging – occur due to perfusion abnormalities but can be difficult to distinguish from HCC.

Management:

Treatment of the underlying cause

Anticoagulation – Not DOAC (lifelong) +/- stent/angioplasty +/- TIPSS +/- transplantation

Portal vein thrombosis (PVT)

A local cause (e.g cirrhosis, malignancy, inflammation) is more commonly seen than in BCS. The prevalence of PVT is 0.6-5% in compensated liver disease and 40% in patients awaiting transplantation (3 monthly USS recommended in those being assessed/ waiting for transplantation). Mortality from variceal haemorrhage is increased in those with PVT complicating cirrhosis (36 vs 16% at 6 weeks).

Acute PVT

***Presentation*:** ranges from asymptomatic to intestinal infarction. May be unprovoked or in the setting of HPB disease such as acute pancreatitis.

- Classic symptoms - abdominal pain (90%), systemic inflammation - fever, raised CRP/ ESR (85%)
- LFTs - generally normal or mild transaminitis
- Ascites present in 50%, but usually only evident on imaging
- **Intestinal infarction** - pain, bloody diarrhoea, raised lactate and metabolic acidosis (occurs if extension of thrombus into mesenteric veins leads to rapid and complete obstruction before formation of collateral circulation) – treatment laparotomy, mortality 60%
- Pyophlebitis (acute septic PVT) is characterised by fever, rigors and right upper quadrant pain. Complications include multiple liver abscesses

Management: Prompt anticoagulation is essential to reduce the risk of clot extension. Involve surgeons and critical care early if intestinal ischaemia is suspected radiologically/clinically. There is limited data on the use of direct mechanical thrombectomy via TIPSS– consider discussion with specialist transplant centre if significant clot burden or progression despite systemic anticoagulation.

Anticoagulation – patients with acute PVT require a minimum 6 months. This duration is indicated in the setting of a clear provoked event such as pancreatitis. Lifelong anticoagulation is indicated if

permanent strong prothrombotic or myeloproliferative condition or intestinal ischaemia. Recanalisation after 6-12 months occurs in 39% portal vein, 80% splenic and 73% SMV thromboses.

Chronic PVT

Portal cavernoma (network of hepatopetal collaterals) fully develops in ~ 2 months

Presentation

- 90% present with a variceal bleed; less commonly with ascites or encephalopathy
- Hepatic decompensation in presence of cirrhosis

Management:

1. Treatment of the underlying cause
2. Surveillance and management of varices as in cirrhosis - see varices surveillance guideline
3. Anticoagulation – In chronic PVT anticoagulation should be considered on an individual case basis and after screening +/- treatment for varices
   In PVT with cirrhosis: any transplant-listed patients should be discussed promptly with the transplant centre but the majority are anticoagulated to prevent clot extension and consequent inoperability. In non-listed patients, anticoagulation is limited to those with symptoms (e.g abdo pain or worsening ascites) or with other risks factors for thrombosis. Typically patients who have cavernoma formation at diagnosis will not require anticoagulation. Avoid if platelet count <50.
   In PVT without cirrhosis: lifelong anticoagulation is indicated if history of other thromboses, permanent strong prothrombotic or myeloproliferative condition.

Currently anticoagulation with either low-molecular weight heparin or warfarin is recommended. There are insufficient data to support the use of DOACs for this indication.

Sinusoidal Obstruction Syndrome (SOS)

Sinusoidal obstruction which may extend to the level of the central vein

Causes:

- Myeloablative regimens (high dose chemotherapy +/- total body irradiation) used prior to haematopoietic stem cell transplantation (HSCT) – incidence has ↓ due to prophylaxis (defibrotide), lower radiation doses and less reliance on cyclophosphamide
- Other chemotherapeutic agents e.g cyclophosphamide
- Immunosuppressive therapy (e.g. azathioprine, 6-mercaptopurine)
- Ingestion of herbal teas made with pyrrolizidine alkaloids e.g Jamaican bush tea

Presentation:

Onset typically 10-20/7 after cyclophosphamide or >30/7 after myeloablative therapy.

- Weight gain with or without detectable ascites
- Hepatomegaly (tender)
- Jaundice and ultimately liver failure and death.

Diagnosis:

- Transjugular Liver biopsy (with HVPG measurement - supportive if > 10mmHg in patient post HSCT). Primary histological feature is centrilobular necrosis

Management:

- Supportive management is the mainstay of therapy
- Transplantation if there is a favourable prognosis relating to the original disease

(Idiopathic) non-cirrhotic portal hypertension

Requires exclusion of infiltrative disease, haematological malignancy, thrombophilia, schistosomiasis, HIV, congenital hepatic fibrosis, sarcoidosis and drug causes (e.g Azathioprine).

Presentation:

- GI haemorrhage secondary to portal hypertension
- Splenomegaly
- LFTs usually normal at initial diagnosis
- Ascites (poor prognostic sign)

Diagnosis:

- Liver biopsy – phlebosclerosis, nodular regenerative hyperplasia, sinusoidal dilatation, paraseptal shunt vessels, perisinusoidal fibrosis

Management:

- Surveillance and management of varices as in cirrhosis- see varices surveillance guideline

- Anticoagulation not recommended unless underlying prothrombotic disorder
- USS looking for PVT 6 monthly

Further reading: EASL Clinical Practice Guidelines: Vascular diseases of the liver. Journal of Hepatology 2015
AASLD practice guidelines: Vascular disorders of the liver 2020

Documentation Controls (these go at the end of the document but before any appendices)

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<tr><td>Reference Number

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3</td><td>Status

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<tr><td rowspan="3">Version / Amendment History</td><td>Version</td><td>Date</td><td>Author</td><td colspan="2">Reason</td></tr>
<tr><td>3</td><td>2022</td><td>Liver Management Group (cross-site teams)</td><td colspan="2">Previous version of guideline expired</td></tr>
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<tr><td colspan="5">Intended Recipients: All clinicians managing patients with liver disease</td></tr>
<tr><td colspan="5">Training and Dissemination: Forms part of liver handbook which is disseminated to all clinicians rotating through Hepatology</td></tr>
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Job Title: Dr A Lawson (Consultant Hepatologist)</td></tr>
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