Is there still a role for surgery in non cirrhotic portal hypertension?

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Una chirurgia in estinzione?
1. Rivascularization procedures → Meso-Rex Shunt

2. Portosystemic shunts

   Non-Selective:
   - Total:
     - End-to-side portacaval shunt (Eck’s fistula)
     - Side-to-side portacaval shunt (> 10 cm)
     - Mesocaval with prothesesic interposition
     - Proximal splenorenla shunt (Linton’s shunt)
   - Partial:
     - Small diameter end-to-side (8-10 cm)
     - Calibrated side-to-side portacaval shunt
   - Selective:
     - Distal splenorenal shunt (Warren’s shunt)
     - Coronaro-caval anastomosis (abandoned)
     - Spleno-caval anastomosis (abandoned)

3. Devascularization procedures

4. Orthotopic Liver Transplantation
Research performed on PubMed
Main causes of NCPH

Table 1. Causes of Non-cirrhotic portal hypertension (NCPH).

<table>
<thead>
<tr>
<th>Pre-hepatic</th>
<th>Sinusoidal</th>
<th>Post-sinusoidal</th>
</tr>
</thead>
<tbody>
<tr>
<td>FHVP normal, RAP normal, WHVP normal, HVPG normal, PVP high, ISP high</td>
<td>Sinusoidal fibrosis</td>
<td>Venoocclusive disease</td>
</tr>
<tr>
<td>Extrahepatic portal vein obstruction (EHPVO)</td>
<td></td>
<td>Hepatic irradiation</td>
</tr>
<tr>
<td>Portal vein thrombosis</td>
<td>Alcoholic hepatitis</td>
<td>Toxins-Pyrrolizidine alkaloids</td>
</tr>
<tr>
<td>Splenic vein thrombosis</td>
<td>Drugs (methotrexate, amiodarone)</td>
<td>Drugs-Gemtuzumab, ozogamicin, actinomycin D, dacarbazine, cytocide</td>
</tr>
<tr>
<td>Splanchnic arteriovenous fistula</td>
<td></td>
<td>arabinoside, mithramycin, 6-thioguanine, azathioprine, busulfan plus</td>
</tr>
<tr>
<td>Massive splenomegaly</td>
<td></td>
<td>cyclophosphamide</td>
</tr>
<tr>
<td>Infiltrative diseases-Lymphoma, myeloproliferative disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Storage diseases-Gaucher’s disease</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hepatic</th>
<th>Sinusoidal</th>
<th>Post-sinusoidal</th>
</tr>
</thead>
<tbody>
<tr>
<td>FHVP normal, RAP normal, WHVP high, HVPG normal or high, PVP high, ISP high</td>
<td>Sinusoidal fibrosis</td>
<td>Venoocclusive disease</td>
</tr>
<tr>
<td>Neoplastic occlusion of portal vein</td>
<td>Sinusoidal defenestration</td>
<td>Alcoholic liver disease</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>Alcoholic liver disease (early phase)</td>
<td>Chronic radiation injury</td>
</tr>
<tr>
<td>Epithelial hemangiendothelioma</td>
<td>Sinusoidal infiltration</td>
<td>Hypervitaminosis A</td>
</tr>
<tr>
<td>Epithelial malignancies</td>
<td>Mastocytosis</td>
<td>E-ferol injury</td>
</tr>
<tr>
<td>Chronic lymphocytic leukemia</td>
<td>Agnogenic myeloid metaplasia</td>
<td></td>
</tr>
<tr>
<td>Granulomatous lesions</td>
<td>Gaucher’s disease</td>
<td>Primary vascular malignancies</td>
</tr>
<tr>
<td>Schistosomiasis</td>
<td>Amyloidosis</td>
<td>Epithelial hemangiendothelioma</td>
</tr>
<tr>
<td>Mineral oil granuloma</td>
<td>Sinusoidal compression</td>
<td>Angiosarcoma</td>
</tr>
<tr>
<td>Sarcoidsis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatoportal sclerosis</td>
<td>By enlarged Kupffer cells (Gaucher’s disease, visceral Leishmaniasis)</td>
<td>Mycobacterium species</td>
</tr>
<tr>
<td>Peliosis hepatitis</td>
<td>By enlarged fat-laden hepatocytes (Alcoholic hepatitis, AFLP)</td>
<td>Lipogranulomas</td>
</tr>
<tr>
<td>Partial nodular transformation (NCPF)/Idiopathic portal hypertension (IPH)</td>
<td></td>
<td>Mineral oil granuloma</td>
</tr>
<tr>
<td>Post-hepatic</td>
<td>Sinusoidal fibrosis</td>
<td>Hepatic vein outflow tract obstruction (HVOTO, Budd-Chiari syndrome)-Idiopathic, prothrombotic states</td>
</tr>
<tr>
<td>Inferior vena cava obstruction-web, thrombosis, tumour, enlarged caudate lobe</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Constrictive pericarditis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tricuspid regurgitation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe right-sided heart failure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Restrictive cardiomyopathy</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Khanna R et al, J Hepatol 2014 vol. 60; 421–441
NCPH: Associated disorders

Immunological/Autoimmune disorders
• Common variable immunodeficiency syndrome
• Primary antibody-deciency syndrome
• Connnetive tissue diseases
• Crohn’s disease
• Rheumatoid arthritis
• Systemic lupus erythematosus
• Systemic sclerosis
• Scleroderma
• Celiac disease
• Solid organ transplant

Infections
• Bacterial intestinal infections
• HIV infection

Medications/Toxins
• Thiopurine derivatives
• Arsenicals
• Vitamin A
• Chemotherpy

Prothrombotic conditions
• Inherited thrombophilias
• Myeloproliferative neoplasm
• Antiphospholipid syndrome
• Protein S or C deficiency
• Lupus anticoagulant
• Factor V Leiden
• Prothrombin mutation

Hematologic disease
• Myeloproliferative disorders
• Myeloid metaplasia
• Lymphoproliferative conditions
• Spherocytosis

Genetic disorders
• Adams-Olivier Syndrome
• Cystic fibrosis
• Turner’s disease
• Phosphomannose isomerase deficiency
• Familial cases

### Patophysiology as clinical guide

<table>
<thead>
<tr>
<th></th>
<th>Pre-Hepatic</th>
<th>Hepatic</th>
<th>Post-Hepatic</th>
</tr>
</thead>
<tbody>
<tr>
<td>FHVP</td>
<td>Normal</td>
<td>Normal</td>
<td>High</td>
</tr>
<tr>
<td>RAP</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal or High</td>
</tr>
<tr>
<td>WHVP</td>
<td>Normal</td>
<td>High</td>
<td>High</td>
</tr>
<tr>
<td>HVPG</td>
<td>Normal</td>
<td>Normal or High</td>
<td>Normal or High</td>
</tr>
<tr>
<td>PVP</td>
<td>High</td>
<td>High</td>
<td>High</td>
</tr>
<tr>
<td>ISP</td>
<td>High</td>
<td>High</td>
<td>High</td>
</tr>
</tbody>
</table>

FHVP $\rightarrow$ Free hepatic venous pressure  
RAP $\rightarrow$ Right atrial pressure  
WHVP $\rightarrow$ Wedged hepatic venous pressure  
HVPG $\rightarrow$ FHVP – WHVP  
PVP $\rightarrow$ Portal vein pressure  
ISP $\rightarrow$ Intrasplenic pressure

Khanna R et al, J Hepatol 2014 vol. 60; 421–441
Extra Hepatic Portal Vein Obstruction (EHPVO)
NCPH: NCPF and EHPVO
The unifying hypothesis (Sarin and Kumar, 2006)
## EHPVO

### Clinical Features

<table>
<thead>
<tr>
<th>NCPF</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Size of vessel involved</strong></td>
<td></td>
</tr>
<tr>
<td>Hematemesis/melena</td>
<td>77%</td>
</tr>
<tr>
<td>Splenomegaly</td>
<td>20%</td>
</tr>
<tr>
<td>Ascites (transient)</td>
<td>23%</td>
</tr>
<tr>
<td>Jaundice</td>
<td>23%</td>
</tr>
<tr>
<td>Esophageal varices</td>
<td>93%</td>
</tr>
<tr>
<td>Portal gastropathy</td>
<td>60%</td>
</tr>
<tr>
<td>Portal biliopathy</td>
<td>90%</td>
</tr>
<tr>
<td>Other clinical features</td>
<td></td>
</tr>
<tr>
<td>Growth faltering, impaired QoL, minimal hepatic encephalopathy, hypersplenism, splenic infarction, bleeding from non-GI sites: 20%</td>
<td></td>
</tr>
<tr>
<td>Liver function</td>
<td>Preserved</td>
</tr>
</tbody>
</table>

Mean number of 1.8–3.1 bleeding episodes

Splenic size and portal pressure do not correlate with the incidence or severity of bleed.

Liver is normal or shrunken.

Jaundice due to portal biliopathy.

Peripheral stigmata of CLD are absent

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Khanna R et al, J Hepatol 2014 vol. 60; 421–441
Schouten JNL et al, Hepatology 2011;54:1071-1081
EHPVO: Management

Diagnosis of EHPVO
- Splenomegaly, well-terated variceal bleed
- Preserved liver functions
- Growth failure
- Presence of portal cavernoma on USG Doppler
  ± liver biopsy to exclude intrinsic liver disease

History of upper GI bleed

No upper GI bleed
- Primary prophylaxis

Esophagogastroduodenoscopy (EGD)

Situs of bleed

Large esophageal vx
- Small esophageal vx with RCS

Yes

Consider EVL till eradication or beta-blocker

Small eso vx (without RCS), GOV1 or GOV2

IGV

Eradication

Consider shunt surgery

EGD every 2 yr

Colonopaty/rectal varices

Complicated portal biliopathy
- Severe Hypersplenism
- Growth retardation/QoL

Treatment failure

History of umbilical vein catheterization
- Umbilical or neonatal sepsis
- Abdominal trauma/surgery
- Pancreatitis/appendicitis
- Liver abscess

Hemogram,
- Liver function tests
- Coagulation profile,
- Prothrombotic work-up
- Serum homocysteine levels,
- PNH panel

Decrease GOV1
- May decrease GOV2
- Increase IGV1
- Increase PHG
- Increase ectopic vx

Eosophageal vx

Gastric vx

PHG

Ectopic vx
- Duodenal Antral

Consider EVL till eradication or beta-blocker

Small eso vx (without RCS), GOV1 or GOV2

EGD every 2 yr

IGV

Colonopaty/rectal varices

Complicated portal biliopathy
- Severe Hypersplenism
- Growth retardation/QoL

Treatment failure

Khanna R et al, J Hepatol 2014 vol. 60; 421–441
Surgical interventions for PH
Revascularization: MRB
Surgical interventions for PH
Revascularization: MRB

..or, alternatively, splenorenal shunt
Meso-Rex Bypass—A Procedure to Cure Prehepatic Portal Hypertension: The Insight and the Inside

Di Francesco F et al, J AM Coll Surg 2014; 218(2)
Pre-operative assessments:

- Adult and/or pediatric hepatologist
- Cardiologist (to exclude HPS and PPH)
- Hematologist (for prothrombotic states)
- Radiologist (CT/MR angiography/Portography)
Advantages of the Meso-Rex Bypass Compared with Portosystemic Shunts in the Management of Extrahepatic Portal Vein Obstruction in Children

81 children with idiopathic EHPVO evaluated
Between 1997 and 2010
Single Institution

65 underwent successful MRB
16 required PSS

<table>
<thead>
<tr>
<th></th>
<th>MRB</th>
<th>PSS</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relief of variceal bleeding</td>
<td>96%</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>Improvement in PTLS count</td>
<td>+82.1 ± 60.0</td>
<td>+32.4 ± 56.3</td>
<td>0.004</td>
</tr>
<tr>
<td>INR</td>
<td>-0.22 ± 0.27</td>
<td>0.01 ± 0.14</td>
<td>0.022</td>
</tr>
<tr>
<td>Ammonia</td>
<td>-26.8 ± 36.8</td>
<td>+19.4 ± 33.1</td>
<td>0.002</td>
</tr>
<tr>
<td>Improvement in weight/age z-score</td>
<td>+0.84 ± 0.98</td>
<td>+0.17 ± 0.79</td>
<td>0.044</td>
</tr>
</tbody>
</table>

Both MRB and PSS effectively relieve symptoms of portal hypertensive bleeding. MRB relieves hypersplenism better than PSS.

By restoring normal portal venous circulation, the meso-Rex bypass has additional metabolic benefits.
## Portal Biliopathy

Cholangiographic abnormalities which occur in patients with portal cavernoma
First described in early 90’s

### Table 1  Reported studies of portal biliopathy

<table>
<thead>
<tr>
<th>Ref.</th>
<th>Year of publication</th>
<th>City Country</th>
<th>Number of patients</th>
<th>Age (mean)</th>
<th>Male: Female</th>
<th>Biliary changes</th>
<th>Symptomatic disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Khuroo et al[3]</td>
<td>1993</td>
<td>Kashmir India</td>
<td>21</td>
<td>14.0</td>
<td>13:8</td>
<td>81%</td>
<td>38%</td>
</tr>
<tr>
<td>Dilawari et al[6]</td>
<td>1992</td>
<td>Chandigarh India</td>
<td>20</td>
<td>22.0</td>
<td>16:4</td>
<td>100%</td>
<td>5%</td>
</tr>
<tr>
<td>Sarin et al[7]</td>
<td>1992</td>
<td>Delhi India</td>
<td>20</td>
<td>-</td>
<td>16:4</td>
<td>90%</td>
<td>15%</td>
</tr>
<tr>
<td>Bayraktar et al[8]</td>
<td>1995</td>
<td>Ankara Turkey</td>
<td>44</td>
<td>31.5</td>
<td>24:20</td>
<td>94%</td>
<td>30%</td>
</tr>
<tr>
<td>Malik et al[9]</td>
<td>1999</td>
<td>Mumbai India</td>
<td>20</td>
<td>23.0</td>
<td>12:08</td>
<td>85%</td>
<td>10%</td>
</tr>
<tr>
<td>Nagi et al[10]</td>
<td>2000</td>
<td>Chandigarh India</td>
<td>43</td>
<td>-</td>
<td>25:18</td>
<td>100%</td>
<td>19%</td>
</tr>
<tr>
<td>Condat et al[11]</td>
<td>2003</td>
<td>Paris France</td>
<td>25</td>
<td>49.5</td>
<td>15:1</td>
<td>84%</td>
<td>28%</td>
</tr>
<tr>
<td>Sezgin et al[12]</td>
<td>2003</td>
<td>Mersin Turkey</td>
<td>36</td>
<td>-</td>
<td>-</td>
<td>94%</td>
<td>10%</td>
</tr>
<tr>
<td>Khare et al[13]</td>
<td>2005</td>
<td>Lucknow India</td>
<td>13</td>
<td>-</td>
<td>9:4</td>
<td>100%</td>
<td>100%</td>
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<tr>
<td>Belhadjbrk et al[14]</td>
<td>2006</td>
<td>Tunis Tunisia</td>
<td>17</td>
<td>-</td>
<td>-</td>
<td>100%</td>
<td>82%</td>
</tr>
<tr>
<td>Chevallier et al[15]</td>
<td>2006</td>
<td>Nice Cedex 3 France</td>
<td>10</td>
<td>-</td>
<td>-</td>
<td>90%</td>
<td>40%</td>
</tr>
<tr>
<td>Dhiman et al[16]</td>
<td>2007</td>
<td>Chandigarh India</td>
<td>53</td>
<td>24.5</td>
<td>36:17</td>
<td>100%</td>
<td>24.5%</td>
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<tr>
<td>Vibert et al[17]</td>
<td>2007</td>
<td>Villejuif France</td>
<td>64</td>
<td>-</td>
<td>-</td>
<td>100%</td>
<td>30%</td>
</tr>
<tr>
<td>Oo et al[18]</td>
<td>2009</td>
<td>Birmingham UK</td>
<td>13</td>
<td>-</td>
<td>-</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Jloa et al[19]</td>
<td>2011</td>
<td>Barcelona Spain</td>
<td>67</td>
<td>47.0</td>
<td>41:26</td>
<td>78%</td>
<td>21%</td>
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<tr>
<td>Agarwal et al[20]</td>
<td>2011</td>
<td>New Delhi India</td>
<td>39</td>
<td>29.6</td>
<td>27:11</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Aguirre et al[21]</td>
<td>2012</td>
<td>Bogota Columbia</td>
<td>18</td>
<td>-</td>
<td>-</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Aguilar-Olivas et al[22]</td>
<td>2014</td>
<td>DF Mexico</td>
<td>4</td>
<td>-</td>
<td>-</td>
<td>100%</td>
<td>100%</td>
</tr>
</tbody>
</table>

Khuroo MS et al, World J Gastroenterol 2016 September 21; 22(35): 7973-7982
Anatomical consideration in portal biliopaty

CBD draining veins are arranged in the form of two plexuses

Epicholedochal venous plexus (Saint, 1971)
is a fine reticular plexus on the surface of the bile ducts

Paracholedochal venous plexus (Petren, 1932)
lies outside the bile ducts and courses parallel to the ducts
Portal Cavernoma development

PC develops as a bunch of hepatopetal collaterals in response to portomesenteric venous obstruction

Normally:

• PSPDV drains into PV close to porta hepatis

• PSPDV connects with PIPDV which drains into SMV through first jejunal vein (FJV)

Chittapuram SRB et al, J Clin Exp Hepatol 2014;4:S18–S26
Portal Cavernoma development

PC develops as a bunch of hepatopetal collaterals in response to portomesenteric venous obstruction.

Normally:
- PSPDV drains into PV close to porta hepatis
- PSPDV connects with PIPDV which drains into SMV through first jejunal vein (FJV)

PSPDV and Pericholedochal venous plexus dilate and acts as a porto-portal collateral channels → Cavernoma

Chittapuram SRB et al, J Clin Exp Hepatol 2014;4:S18–S26
Portal biliopathy

PC → Subepithelial varices in the CBD wall

Application of color and spectral Doppler shows presence of varices with venous flow in the CBD between the lumen of the CBD and the varices

Chittapuram SRB et al, J Clin Exp Hepatol 2014;4:S18–S26
Sharma M et al, Gastrointest Endosc. 2009;70(5):1041–1043
Denys A et al, AJR. 1998;171:455–456
Portal biliopaty

PC → Subepithelial varices in the CBD wall

Dilatation of large paracholedochal veins

Compression and distortion of the extrahepatic BD with varicoid portal biliopaty (REVERSIBLE)

Enlargement of smaller intramural epicholedochal plexus compromises the arterial supply of the ductal wall producing ischemic changes and fibrosis (IRREVERSIBLE)

Chittapuram SRB et al, J Clin Exp Hepatol 2014;4:S18–S26
Sharma M et al, Gastrointest Endosc. 2009;70(5):1041–1043
Denys A et al, AJR. 1998;171:455–456
Portal Biliopathy Classification

A. Type I, involvement of extrahepatic bile duct
B. Type II, involvement of intrahepatic bile ducts only
C + D. Type IIIa, involvement of extrahepatic bile duct and unilateral intrahepatic bile duct (left or right)
E. Type IIIb, involvement of extra-hepatic bile duct and bilateral intrahepatic ducts.

Khanna R et al, J Hepatol 2014 vol. 60; 421–441
<table>
<thead>
<tr>
<th>Author</th>
<th>Pts N*</th>
<th>Follow-up</th>
<th>Further treatments</th>
<th>Complications/Outcomes</th>
<th>Morbidity</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bhatia et al, 1995</td>
<td>4</td>
<td>3-8 months</td>
<td>Multiple ERCP 4</td>
<td>None</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Perlemuter et al, 1996</td>
<td>8</td>
<td>6-60 months</td>
<td>Multiple ES 1</td>
<td>Death 2 (cholangitis + stroke)</td>
<td>NA</td>
<td>25%</td>
</tr>
<tr>
<td>Condat et al, 2003</td>
<td>7</td>
<td>4-25 months</td>
<td>-</td>
<td>Haemobilia 1</td>
<td>14.3%</td>
<td>0%</td>
</tr>
<tr>
<td>Sezgin et al, 2003</td>
<td>10</td>
<td>3.3 years (1-7)</td>
<td>Multiple ERCP 5</td>
<td>Haemobilia 1 Cholangitis 5 Death 1</td>
<td>60%</td>
<td>10%</td>
</tr>
<tr>
<td>Dumortier et al, 2003</td>
<td>6</td>
<td>10 months (2-18)</td>
<td>Multiple ERCP + PSS 4</td>
<td>Cholangitis 1 Cholecistytis 4</td>
<td>83.3%</td>
<td>0%</td>
</tr>
<tr>
<td>Khare et al, 2005</td>
<td>13</td>
<td>-</td>
<td>PSS 8, BA 1, Multiple ERCP 2, Sugiura 2</td>
<td>Death 1</td>
<td>NA</td>
<td>7.6%</td>
</tr>
<tr>
<td>Dhiman et al, 2007</td>
<td>12</td>
<td>19 months (6-132)</td>
<td>Multiple ERCP</td>
<td>Cholangitis 2</td>
<td>16.6%</td>
<td>0%</td>
</tr>
<tr>
<td>Vibert et al, 2007</td>
<td>19</td>
<td>8.3 years</td>
<td>PSS: BA 5; Non PSS: PTBD 1 after ERCp 4 after BA</td>
<td>Death 3</td>
<td>NA</td>
<td>15.7%</td>
</tr>
<tr>
<td>Oo et al, 2009</td>
<td>13</td>
<td>2 years (1-18)</td>
<td>Stent 3, Stent exchange 2 TIPS 2, PSS 1, LT 1</td>
<td>Haemobilia 2 Sepsis 3</td>
<td>38.5%</td>
<td>0%</td>
</tr>
<tr>
<td>Llop et al, 2011</td>
<td>14</td>
<td>-</td>
<td>Multiple ERCP 1 BA 1</td>
<td>-</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Sarasvat et al, 2013</td>
<td>20</td>
<td>18 months (3-188)</td>
<td>Multiple ERCP 11</td>
<td>In 130 procedures: Cholangitis 40, Haemobilia 9</td>
<td>37.7%*</td>
<td>0%</td>
</tr>
<tr>
<td>Ramchandani et al, 2013</td>
<td>5</td>
<td>6-7 months</td>
<td>SRS 2 Stent exchange 1</td>
<td>-</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Cellich et al, 2015</td>
<td>9</td>
<td>-</td>
<td>PSS 1, BA 3, Stent exchange 3</td>
<td>Cholangitis 3 Haemobilia 1</td>
<td>44%</td>
<td>0%</td>
</tr>
</tbody>
</table>

Modified from Franceschet I et al, World J Gastroenterol 2016 December 7; 22(45): 9909-9920
EHPVO with Portal biliopathy: Algorithm for management

**EHPVO with portal biliopathy**

- Biliary symptoms (fever, jaundice, pain, abdomen)
- Dilated IHBR on USG
- Isolated elevation of SAP (>3 times upper limit of normal for 6-8 wk)

1. **Urgent ERCP**
   - Biliary decompression with stent or endoscopic nasobiliary drainage

2. **ERCP**
   - **Stone in CBD**
     - Present: Stone extraction during ERCP with sphincterotomy
     - Absent: Follow-up
   - Stricture
     - Absent: Mild changes
     - Present: Dominant stricture
       - **Biliary obstruction persists**
         - **Shunt surgery**
           - Long term endoscopic biliary stent placement
           - Biliary diversion surgery (hepatojunostomy or choledochojunostomy)

   - **Balloon dilatation and stenting**
     - Failure
       - **Shuntable vein present**
         - Yes: Shuntable vein placement
         - No: Long term endoscopic biliary stent placement

Khanna R et al, J Hepatol 2014 vol. 60; 421–441
Management of Portal Biliopathy

Unsuccessful vascular surgery is frequent in mixed type because of co-presence of ischemic and compressive damage.

Franceschet I et al, World J Gastroenterol 2016 December 7; 22(45): 9909-9920
## Portal Biliopathy Classification: Surgical Management

<table>
<thead>
<tr>
<th>Author</th>
<th>Pts N°</th>
<th>Follow-up</th>
<th>Treatments</th>
<th>Further Treatments</th>
<th>Morbidity</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chaudhary et al, 1998</td>
<td>9</td>
<td>-</td>
<td>BA2, SRS 7</td>
<td>BA 2, Stent 1, ES + SE 2</td>
<td>NA</td>
<td>11.1%</td>
</tr>
<tr>
<td>Condat et al, 2003</td>
<td>7</td>
<td>4-25 months</td>
<td>Cholecistectomy + ERCP 1, stent 1, BA + PTBD 1</td>
<td>-</td>
<td>14.3%</td>
<td>0%</td>
</tr>
<tr>
<td>Gauthier-Villars et al, 2005</td>
<td>8</td>
<td>4.5-15 ys</td>
<td>PSS 8</td>
<td>-</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Khare et al, 2005</td>
<td>13</td>
<td>-</td>
<td>PSS 7, BA1 , ERCP 6, BA + PSS 1, Sugiura 2</td>
<td>ERCP 1, Splenectomy, ERCP 2; BA 1; Splenectomy + BA 1</td>
<td>NA</td>
<td>1.9%</td>
</tr>
<tr>
<td>Vibert et al, 2007</td>
<td>19</td>
<td>4-30 months</td>
<td>PTBD 1, SRS 10</td>
<td>BA 5, PTBD 5</td>
<td>NA</td>
<td>15.7%</td>
</tr>
<tr>
<td>Dhiman et al, 2007</td>
<td>12</td>
<td>19 months (6-132)</td>
<td>Stent 2, stone extraction 1, PTBD 6, BA 4</td>
<td>Multiple stent exchange</td>
<td>16.6%</td>
<td>NA</td>
</tr>
<tr>
<td>D’Souza et al, 2009</td>
<td>1</td>
<td>18 months</td>
<td>PSS 5, ES 3, ES + dilatation 2, stent 4</td>
<td>-</td>
<td>NA</td>
<td>0%</td>
</tr>
<tr>
<td>Camerlo et al, 2010</td>
<td>3</td>
<td>2-13 years</td>
<td>PSS 3, stent 1</td>
<td>-</td>
<td>NA</td>
<td>0%</td>
</tr>
<tr>
<td>Argawal et al, 2011</td>
<td>39</td>
<td>32 months</td>
<td>SRS 37, BA 2</td>
<td>ES + SE 10, BA 12, ES + cholecistectomy</td>
<td>NA</td>
<td>0%</td>
</tr>
<tr>
<td>Chattopadhyay et al, 2012</td>
<td>56</td>
<td>48 months (14-120)</td>
<td>40 PSS + 16 Sugiura</td>
<td>ES + SE 2, Multiple ES + Stent 5, BA 2</td>
<td>NA</td>
<td>4.2%</td>
</tr>
<tr>
<td>Suarez et al, 2013</td>
<td>3</td>
<td>-</td>
<td>UDCA 1, BA 1</td>
<td>-</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Bhatia et al, 2014</td>
<td>2</td>
<td>-</td>
<td>Cholecistectomy</td>
<td>-</td>
<td>NA</td>
<td>0%</td>
</tr>
<tr>
<td>Liu et al, 2015</td>
<td>18</td>
<td>-</td>
<td>PSS 18</td>
<td>-</td>
<td>NA</td>
<td>0%</td>
</tr>
</tbody>
</table>

Modified from Franceschet I et al, World J Gastroenterol 2016 December 7; 22(45): 9909-9920
NCPH: Non Cirrhotic Portal Fibrosis (OPV)

Microscopic features in cases of pure NCPF group (Masson trichrome stain)

<table>
<thead>
<tr>
<th>Fibrous intimal thickening of medium size portal vein (PV)</th>
<th>Portal fibrosis with complete obliteration or multichannelling of PV branches</th>
</tr>
</thead>
</table>

![Microscopic features](image-url)

**NCPH: PRE-sinusoidal**  
**NCPF and EHPVO**

<table>
<thead>
<tr>
<th></th>
<th>NCPF</th>
<th>EHPVO</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean age (y)</strong></td>
<td>31</td>
<td>19.4</td>
</tr>
<tr>
<td><strong>Sex (Males/Females)</strong></td>
<td>1 : 0.7</td>
<td>1 : 0.5</td>
</tr>
<tr>
<td><strong>Geographical distribution</strong></td>
<td>&gt; in developing countries</td>
<td>&gt; In developing countries</td>
</tr>
<tr>
<td><strong>Size of vessel involved</strong></td>
<td>Peripheral portal vein branches</td>
<td>Main portal vein</td>
</tr>
<tr>
<td><strong>Hematemesis/melena</strong></td>
<td>82%</td>
<td>77%</td>
</tr>
<tr>
<td><strong>Splenomegaly</strong></td>
<td>21%</td>
<td>20%</td>
</tr>
<tr>
<td><strong>Ascites (transient)</strong></td>
<td>19%</td>
<td>23%</td>
</tr>
<tr>
<td><strong>Jaundice</strong></td>
<td>7.8%</td>
<td>23%</td>
</tr>
<tr>
<td><strong>Esophageal varices</strong></td>
<td>96%</td>
<td>93%</td>
</tr>
<tr>
<td><strong>Portal gastropathy</strong></td>
<td>3.2%</td>
<td>60%</td>
</tr>
<tr>
<td><strong>Portal biliopathy</strong></td>
<td>25%</td>
<td>90%</td>
</tr>
<tr>
<td><strong>Liver function</strong></td>
<td>Preserved</td>
<td>Preserved</td>
</tr>
<tr>
<td><strong>Other clinical features</strong></td>
<td>± hypersplenism, anemia</td>
<td>Growth faltering Minimal hepatic encephalopathy</td>
</tr>
<tr>
<td></td>
<td>Patent hepatic portal vein</td>
<td>Gastropathy, Colopathy</td>
</tr>
<tr>
<td><strong>Prognosis</strong></td>
<td>Fairly good but need for regular and careful surveillance</td>
<td></td>
</tr>
</tbody>
</table>
Endoscopic therapy in NCPH is effective in:

- Controlling acute variceal bleeding in 95% of patients
- Reduce the risk of variceal rebleeding

With uncontrolled bleeding portal systemic shunting by insertion of TIPS should be considered.

Liver transplantation in unmanageable portal hypertension-related complications and progressive liver failure
Indications requiring liver transplantation in these patients were:

- Medical unmanageable portal hypertension
- Hepatopulmonary syndrome
- Hepatic encephalopathy
- Progressive hepatic failure

To prevent unnecessary LT, early discrimination between cirrhosis and INCPH is extremely important.

Based on small-sized cohorts, post-LT outcome in these patients is good and INCPH tends not to recur.

Schouten JNL et al, Hepatology 2011;54:1071-1081
Non Cirrhotic Portal Fibrosis and CLD

Table 2 Relevant pre-LT clinical and other parameters in 10 cases of NCPF related end stage CLD (pure NCPF)

<table>
<thead>
<tr>
<th>No.</th>
<th>Age/sex (years)</th>
<th>Pre-LT diagnosis</th>
<th>Clinical Jaundice</th>
<th>GI Bleed</th>
<th>Enceph</th>
<th>Ascites/ SBP</th>
<th>Variceal grade</th>
<th>MELD score</th>
<th>Metabolic Obesity</th>
<th>BMI (kg/m²)</th>
<th>Diabetes</th>
<th>Systemic HTN</th>
<th>Biochemical Bilirubin (mg/dL)</th>
<th>Albumin (g/dL)</th>
<th>AST (IU/L)</th>
<th>INR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>56/M</td>
<td>CC</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes/yes</td>
<td>2-3</td>
<td>22</td>
<td>No</td>
<td>22.83</td>
<td>No</td>
<td>No</td>
<td>3</td>
<td>2.9</td>
<td>19</td>
<td>1.6</td>
</tr>
<tr>
<td>2</td>
<td>41/M</td>
<td>CC</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes/yes</td>
<td>2-3</td>
<td>23</td>
<td>No</td>
<td>23.8</td>
<td>No</td>
<td>No</td>
<td>1.3</td>
<td>3.4</td>
<td>49</td>
<td>1.68</td>
</tr>
<tr>
<td>3</td>
<td>61/F</td>
<td>CC</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes/yes</td>
<td>2-3</td>
<td>11</td>
<td>No</td>
<td>20</td>
<td>No</td>
<td>No</td>
<td>2</td>
<td>2.8</td>
<td>43</td>
<td>0.91</td>
</tr>
<tr>
<td>4</td>
<td>58/M</td>
<td>CC</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Yes/yes</td>
<td>3</td>
<td>14</td>
<td>No</td>
<td>17.18</td>
<td>Yes</td>
<td>No</td>
<td>1.7</td>
<td>3</td>
<td>38</td>
<td>1.7</td>
</tr>
<tr>
<td>5</td>
<td>56/M</td>
<td>CC</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Yes/yes</td>
<td>3</td>
<td>10</td>
<td>No</td>
<td>14.7</td>
<td>No</td>
<td>No</td>
<td>1</td>
<td>2.4</td>
<td>30</td>
<td>1.39</td>
</tr>
<tr>
<td>6</td>
<td>37/M</td>
<td>CC</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No/yes</td>
<td>3</td>
<td>14</td>
<td>No</td>
<td>17.14</td>
<td>No</td>
<td>No</td>
<td>2.2</td>
<td>3.4</td>
<td>25</td>
<td>1.54</td>
</tr>
<tr>
<td>7</td>
<td>54/M</td>
<td>CC</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes/yes</td>
<td>1</td>
<td>14</td>
<td>No</td>
<td>21.63</td>
<td>No</td>
<td>No</td>
<td>2.3</td>
<td>3.4</td>
<td>44</td>
<td>1.49</td>
</tr>
<tr>
<td>8</td>
<td>56/M</td>
<td>ALC</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes/no</td>
<td>2</td>
<td>12</td>
<td>No</td>
<td>24.09</td>
<td>Yes</td>
<td>No</td>
<td>0.6</td>
<td>4.4</td>
<td>23</td>
<td>1.36</td>
</tr>
<tr>
<td>9</td>
<td>61/F</td>
<td>CC</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes/yes</td>
<td>3</td>
<td>9</td>
<td>No</td>
<td>18.9</td>
<td>Yes</td>
<td>No</td>
<td>1.4</td>
<td>3.4</td>
<td>38</td>
<td>1.43</td>
</tr>
<tr>
<td>10</td>
<td>56/M</td>
<td>CC</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes/no</td>
<td>2</td>
<td>11</td>
<td>No</td>
<td>18.7</td>
<td>Yes</td>
<td>No</td>
<td>0.7</td>
<td>3.3</td>
<td>72</td>
<td>1.25</td>
</tr>
</tbody>
</table>

GI gastrointestinal, Enceph encephalopathy, SBP spontaneous bacterial peritonitis, BMI body mass index, HTN hypertension, AST aspartate amino transferase, INR international normalized ratio, MELD model for end stage liver disease, CC cryptogenic cirrhosis, ALC alcoholic cirrhosis, # intractable ascites

CLD was classified mainly as CC before LT
Non Cirrhotic Portal Fibrosis
Explant pathology

Table 2  Histopathological features in 10 native explant livers finally categorised as NCPF

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Large/medium</th>
<th>Small</th>
<th>Portal fibrosis</th>
<th>Nodular regeneration</th>
<th>Megasinusoids</th>
<th>Peliosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Mild</td>
<td>Moderate</td>
<td>Mild</td>
<td>Absent</td>
<td>Absent</td>
<td>Mild</td>
</tr>
<tr>
<td>2</td>
<td>Mild</td>
<td>Mild</td>
<td>Moderate</td>
<td>Absent</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>3</td>
<td>Severe</td>
<td>Severe</td>
<td>Moderate</td>
<td>Absent</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>4</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Severe</td>
<td>Absent</td>
<td>Mild</td>
<td>Absent</td>
</tr>
<tr>
<td>5</td>
<td>Mild</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Absent</td>
<td>Absent</td>
<td>Mild</td>
</tr>
<tr>
<td>6</td>
<td>Mild</td>
<td>Mild</td>
<td>Mild</td>
<td>Moderate</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>7</td>
<td>Moderate</td>
<td>Mild</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Absent</td>
</tr>
<tr>
<td>8</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Severe</td>
<td>Mild</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>9†</td>
<td>Severe</td>
<td>Mild</td>
<td>Mild</td>
<td>Moderate</td>
<td>Severe</td>
<td>Moderate</td>
</tr>
<tr>
<td>10</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Mild</td>
<td>Absent</td>
<td>Moderate</td>
<td>Absent</td>
</tr>
</tbody>
</table>

*See section on materials and methods for explanation of each histological feature.
†In this liver some large portal vein branches near the hilum had irregular thickened walls and few mural and organising thrombi. NCPF, non-cirrhotic portal fibrosis.

Nayak NC et al, J Clin Pathol 2011;64:592-598
Patients non-responsive to medical treatment not candidates for angioplasty/stenting must be treated with derivative techniques (Shunt/TIPSS)

Transform the portal system into an outflow tract

The most frequent surgical shunt: MESOCAVAAL SHUNT (PTFE stent or autologous jugular vein interposition)

Easier than the Side-to-side PCS because of the hypertrophy of the caudate lobe

IVC thrombosis or severe compression of the IVC? → Meso-atrial shunt → Cavo-atrial shunt + portocaval shunt

Surgical shunts have not demonstrated to be an independent survival advantage in patients with BCS
Budd Chiari Syndrome
AISF Management Algorithm

Senzolo M et al, Digestive and Liver Disease 43 (2011) 503–514
Budd Chiari Syndrome: TIPSS

221 consecutive BCS patients
Multicenter (6 European centers)
Between July 1993 and March 2006

Recanalisation (n=29): No deaths

TIPS eligible (n=147) (66.5%)

Terminal haematological disorders (n=6): All dead

Anticoagulation (n=39): No deaths

Technical contraindications (n=14)
- Portal vein thrombosis
- Severe hepatic dysfunction
- Polycystic liver-kidney disorder
- Iodine contrast allergy
- Death without further Rx.
- OLT, no deaths
- Surgical Shunts, 1 death

TIPS attempted (n=133)

TIPS performed (n=124) (56%)

Technical failure (n=9): 4 deaths without further Rx, 3 OLT, no deaths, 2 Surgical shunt, 1 death
Contraindications to TIPS placement

<table>
<thead>
<tr>
<th>Absolute</th>
<th>Relative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary prevention of variceal bleeding</td>
<td>Hepatocellular carcinoma, especially central</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>Obstruction of all hepatic veins</td>
</tr>
<tr>
<td>Severe tricuspid regurgitation</td>
<td>Portal vein thrombosis</td>
</tr>
<tr>
<td>Severe pulmonary hypertension</td>
<td>Moderate pulmonary hypertension</td>
</tr>
<tr>
<td>Multiple hepatic cysts</td>
<td>Severe coagulopathy (international normalized ratio &gt; 5)</td>
</tr>
<tr>
<td>Uncontrolled systemic infection or sepsis</td>
<td>Thrombocytopenia of &lt; 20,000 cells/cm³</td>
</tr>
<tr>
<td>Unrelieved biliary obstruction</td>
<td>Hepatic encephalopathy</td>
</tr>
</tbody>
</table>

Contraindications of TIPS placement are not necessary applicable to surgical shunts:

Could indication to PSS be extended over tips indications?

Fidelman et al, AJR 2012; 199:746–755
The Evolution of Portal Hypertension Surgery
Lessons From 1000 Operations and 50 Years’ Experience

Héctor Orozco, MD; Miguel Angel Mercado, MD

<table>
<thead>
<tr>
<th>Variable</th>
<th>DSRS</th>
<th>LDMS</th>
<th>Mesorenal or Mesocaval</th>
<th>Proximal Splenorenal</th>
<th>Portacaval</th>
<th>Sugiuara-Futagawa</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients period</td>
<td>296</td>
<td>37</td>
<td>27</td>
<td>38</td>
<td>103</td>
<td>27 One-stage and 251 abdominal-stage</td>
</tr>
<tr>
<td>Operative mortality, %</td>
<td>5/3†</td>
<td>3</td>
<td>10</td>
<td>14</td>
<td>11</td>
<td>6/2†</td>
</tr>
<tr>
<td>Rebleeding, %</td>
<td>6</td>
<td>15</td>
<td>5</td>
<td>11</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Encephalopathy, %</td>
<td>8‡</td>
<td>38</td>
<td>40</td>
<td>40</td>
<td>43</td>
<td>4‡</td>
</tr>
</tbody>
</table>

*DSRS indicates distal splenorenal shunt; LDMS, low-diameter mesocaval shunt.
†Past 5 years.
‡Significant difference (P<.05).
R.S, male, 19 years
PH in Klippel-Tranaunay Syndrome

MH:

Congenital hypothyroidism
1998 Partial removal angioma right thigh
2005 Sclerotherapy of macrocystic

2006 → 2016
Sclerotherapy of lymphatic malformations of the abdominal lower quadrant
Laser treatment of genital/rectal varices

Early July 2016 Upper GI hemorrhage
Oesophageal varices ligation

Liver biopsy: minimal fibrosis with accentuation of portals branches (METAVIR F0) no inflammation portal, steatosis or cholestasis.

Severe bleeding rectal varices
INR 1.38, PT 56%
Total bilirubin 8.8 umol/L
R.S, male, 19 years
PH in Klippel-Tranaunay Syndrome

MH:
Congenital hypothyroidism
1998 Partial removal angioma right thigh
2005 Sclerotherapy of macrocystic

2006 → 2016
Sclerotherapy of lymphatic malformations of the abdominal lower quadrant
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Severe bleeding rectal varices
INR 1.38, PT 56%
Total bilirubin 8.8 umol/L
R.S, male, 19 years
PH in Klippel-Tranaunay Syndrome
R.S, male, 19 years
PH in Klippel-Tranaunay Syndrome

Splenomeseraic carrefour

U Cillo, Personal Experience
R.S, male, 19 years
PH in Klippel-Tranaunay Syndrome

Proximal renal vein
Splenomeseraic carrefour

U Cillo, Personal Experience
R.S, male, 19 years
PH in Klippel-Tranaunay Syndrome

Anastomotic site

U Cillo, Personal Experience
NCPH:
Indication for surgery

The role of surgery is limited to those who fail to respond to medical-endoscopic-radiologic therapy

Absolute:

- Medically/endoscopically refractory variceal hemorrhage
- Symptomatic hypersplenism (recurrent bleeds/infections)
- Platelet count <10,000/mm³
- Symptomatic/Medically refractory HE
- Hepatopulmonary syndrome (HPS)
- Portopulmonary hypertension (PPH)
NCPH: Indication for shunt surgery

The role of surgery is limited to those who fail to respond to medical-endoscopic-radiologic therapy

**Absolute:**
- Medically/endoscopically refractory variceal hemorrhage
- Symptomatic hypersplenism (recurrent bleeds/infections)
- Platelet count <10,000/mm³
- Symptomatic/Medically refractory HE
- Hepatopulmonary syndrome (HPS)
- Portopulmonary hypertension (PPH)

**Relative:**
- Portal biliopathy (PB)
- Symptomatic splenomegaly (pain/rupture/infarction)
- Poor health related QoL
- Large varices with poor access to healthcare or rare blood group
- Patients who desire a one-time treatment
- Refractory lower GI bleed (anorectal varices/colopathy)
- Neurocognitive testing suggesting of MHE
- Growth failure (Z-scores <-2 despite nutritional rehabilitation)
- Delay in sexual development

Superina R et al, Pediatr Transplant 2006;10:908–913

Sarin SK et al, Liver Int 2006;26:512–519
Khanna R et al, J Hepatol 2014 vol. 60; 421–441
Save
the Portal Hypertension
SURGERY!

....and prepare the future portal hypertension SURGEONS!
Storia chirurgia ipertensione portale

PORTAL VEIN HYPERTENSION

Effect of shunt surgery on spleen size, portal pressure and oesophageal varices in patients with non-cirrhotic portal hypertension

86 patients with NCPH
Between 1979 to 1991

56 patients with EHPVO
30 patients with NCPF

Following Side-to-Side Lieno-Renal Shunt (SSLR) there is a significant reduction in SPP and varices

SSLR shunt is effective in the treatment of PH

Table 2 Pre- and postoperative spleen size, splenic pulp pressure (SPP) and oesophageal varices in non-cirrhotic portal fibrosis patients with a patent shunt (n = 28)

<table>
<thead>
<tr>
<th></th>
<th>Before</th>
<th>After</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spleen size (cm BCM)</td>
<td>9.1 ± 3.3</td>
<td>6.8 ± 4.6</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>SPP (cm of saline)</td>
<td>46.3 ± 13.5</td>
<td>33.8 ± 7.6</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Oesophageal varices grade</td>
<td>2.8 ± 0.7</td>
<td>1.05 ± 0.96</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

BCM, below costal margin.

Surgical interventions for PH

1. Rivascularization procedures → Meso-Rex Shunt

2. Portosystemic shunts → Non-Selective:

   **Total:**
   - End-to-side portacaval shunt (Eck's fistula)
   - Side-to-side portacaval shunt (> 10 cm)
   - Mesocaval with prothesic interposition
   - Proximal splenorenal shunt (Linton's shunt)

   **Partial:**
   - Small diameter end-to-side (8-10 cm)
   - Calibrated side-to-side portacaval shunt

   **Selective:**
   - Distal splenorenal shunt (Warren's shunt)
   - Coronaro-caval anastomosis (abandoned)
   - Spleno-caval anastomosis (abandoned)

3. Devascularization procedures

4. Orthotopic Liver Transplantation
Surgical interventions for PH

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     • Spleno-caval anastomosis (abandoned)

3. Devascularization procedures

4. Orthotopic Liver Transplantation
Type of surgical shunt and pathophysiological implications

Non Selective (Central) vs Selective (Periferic) Shunt
Non Selective Total PSS

- End-To-Side PCS
- Side-To-Side PCS
- Proximal Spleno-Renal Shunt (Linton Shunt) + Splenectomy

Non Selective Total PSS

Indications

- Bleeding esophageal or gastric varices unresponsive to other therapies
- Bleeding from portal hypertensive gastropathy unresponsive to pharmacologic therapy
- Budd-Chiari syndrome with patent IVC
- Intractable ascites unresponsive to non-surgical therapy
- Failed TIPS
- Patient not candidates for selective shunt (technical consideration or ascites)

Contraindications

- Extrahepatic portal hypertension
- Portal vein thrombosis not amenable to thrombectomy
- Occlusion of the hepatic artery

Significative decrement in HVPG
Frequent inversion of portal blood flow direction
Persistence of intra-sinusoidal PH
Non Selective Total PSS

Postoperative Complications

Early:
- Hepatic failure
- Renal failure
- Infection
- Gastric acid hypersecretion
- Delirium tremens
- Ascites
- Gastrointestinal bleeding

Late:
- Portasystemic encephalopathy (PSE)
- Liver failure
- Shunt thrombosis
- Hepatocellular carcinoma

In some patients not suited for a selective shunt, a non-selective shunt might serve as a long-term bridge to LT when bleeding is not controlled endoscopically or by TIPS.

Mesocaval or Linton shunts avoiding dissection of hepatic hilum.
Non Selective PSS

- End-To-Side PCS
- Side-To-Side PCS
- Proximal Spleno-Renal Shunt (Linton Shunt) + Splenectomy

Non selective Partial PSS:
- Small diameter end-to-side (8-10 cm)
- Calibrated side-to-side portacaval shunt

Surgical interventions for PH

1. Rivascularization procedures → Meso-Rex Shunt

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3. Devascularization procedures

4. Orthotopic Liver Transplantation
Type of surgical shunt and pathophysiological implications

Selective (Periferic) Shunt

DSRS was an improvement over nonselective shunting procedures.

It preferentially decompresses:
- venous collaterals around the stomach
- venous collateral around the lower esophagus

preventing further hemorrhage

**Compartmentalization of the portal venous circulation**

→ maintains portal blood flow to the liver
→ diminishes the risks of postoperative encephalopathy and accelerated hepatic failure

Ligation of the coronary and gastroepiploic veins separates the high pressure SMV system from the gastro-splenic venous system at least temporarily.

Elwood et al, Arch Surg. 2006;141:385-388
Selective PSS: Distal Spleno-Renal Shunt (Warren's Shunt)

Indications

Bleeding esophageal varices refractory to other treatments
well-preserved hepatic function

Contraindications

Advanced liver disease
Splenic vein thrombosis with no shuntatable vessels < 7 mm
Intractable ascites
Previous splenectomy
Ascites (worsened by DSRS)

Relative contraindications

Progressive liver disease in patients likely to come to transplant
in the next 2–3 years
Small splenic vein
Abnormal anatomy of left renal vein

Blumgart's Surgery of the liver, pancreas and biliary tract, 5th Ed.
EMC – Role of Surgery in the treatment of PH complications – Surgery of PH
A prospective multicenter RCT
- 140 patients, CPT-A/B

DSRS and TIPS are similarly efficacious in the control of refractory variceal bleeding in CPT-A/B

Reintervention is significantly greater for TIPS compared with DSRS

Because both procedures have equivalent outcomes the choice is dependent on available expertise and ability to monitor the shunt and reintervene when needed

<table>
<thead>
<tr>
<th>Costs</th>
<th>P = NS</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-years survival</td>
<td>81%</td>
</tr>
<tr>
<td>5-years survival</td>
<td>62%</td>
</tr>
</tbody>
</table>

Henderson et al, Gastroenterology 2006 May;130(6):1643-51
Differential Effects on Portal and Effective Hepatic Blood Flow
A Comparison Between Transjugular Intrahepatic Portasystemic Shunt and Small-Diameter H-Graft Portacaval Shunt

Table 3. EFFECTS OF SHUNTING ON PORTAL AND EFFECTIVE HEPATIC BLOOD (EHBF) FLOW

<table>
<thead>
<tr>
<th>Shunt Type</th>
<th>Effect on Portal Flow</th>
<th>Effect on Effective Hepatic Flow</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIPS</td>
<td>Increased</td>
<td>Significantly diminished</td>
</tr>
<tr>
<td>HGPCS</td>
<td>Unchanged</td>
<td>Well preserved</td>
</tr>
</tbody>
</table>

- Both TIPS and HGPCS achieved significant reductions in PV → IVC pressure gradients
- Portal flow increased after TIPS, although most portal flow was diverted through the shunt
- Effective hepatic flow is reduced significantly after TIPS but well preserved after HGPCS
- Hepatic decompensation and mortality after TIPS may be because of reductions in nutrient hepatic flow

- **TIPS** → significantly diminished (1684 mL/minute + 2161 to 676 mL/minute ± 451, p < 0.05)
- **HGPCS** → unaffected (1901 mL/minute ± 1818 to 1662 mL/minute ± 1035, p = n.s.)
Mortality after TIPS higher than after HGPCS hepatic failure probably due to excessive diminution of hepatic blood flow

Table 2. BOTH TIPS AND SMALL DIAMETER PROSTHETIC HGPCS ACHIEVED PARTIAL PORTAL DECOMPRESSION

<table>
<thead>
<tr>
<th></th>
<th>TIPS</th>
<th>HGPCS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preshunt PV pressure</td>
<td>33 ± 8.0</td>
<td>31 ± 4.1</td>
</tr>
<tr>
<td>(mm Hg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postshunt PV pressure</td>
<td>26 ± 8.2†</td>
<td>21 ± 4.7†</td>
</tr>
<tr>
<td>(mm Hg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preshunt PV–IVC pressure</td>
<td>18 ± 6.3</td>
<td>16 ± 3.9</td>
</tr>
<tr>
<td>gradients (mm Hg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postshunt PV–IVC pressure</td>
<td>9 ± 3.5†</td>
<td>6 ± 4.5†</td>
</tr>
<tr>
<td>gradients (mm Hg)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

PV = portal vein; IVC = inferior vena cava.
* less than after TIPS p < 0.03, Student’s t-test.
† less than preshunt p < 0.01, paired Student’s t-test.
Data are expressed as mean ± SD.
Surgical interventions for PH

1. Rivascularization procedures → Meso-Rex Shunt

2. Portosystemic shunts

→ Non-Selective:

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3. Devascularization procedures

4. Orthotopic Liver Transplantation
Sugiura Procedure and modifications

Developed to improve the effect of Walker’s simple esophageal transection

1. Esophageal transection
2. Extensive esophago-gastric devascularization
3. Splenectomy
4. Selective vagotomy
5. Piloroplasty

Patients who are unable to undergo shunting procedures nor TIPS because of extensive splanchnic vein thrombosis

Blumgart's Surgery of the liver, pancreas and biliary tract, 5th Ed.
EMC – Role of Surgery in the treatment of PH complications – Surgery of PH
Modified Sugiura procedure remains an effective rescue therapy for patients bleeding patients when alternative treatments fail or are not indicate

It can be a life-saving procedure in:

- Patients with anatomy unsuitable for shunt surgery

- Patients treated in non-specialized centers where surgical expertise for a shunt operation is not available

Surgical interventions for PH

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     - Spleno-caval anastomosis (abandoned)

3. Devascularization procedures

4. Orthotopic Liver Transplantation
From 1972 to 1999
60 patients with BCS divided into three groups:
1. occlusion confined to hepatic veins (n=32) → Direct side-to-side portacaval shunt (SSPCS)
2. occlusion involving the inferior vena cava (IVC) → Portal decompressive procedure that by-passed the obstructed IVC
3. advanced cirrhosis and hepatic decompensation → referred for liver transplantation

SSPCS in BCS with hepatic vein occlusion alone results in reversal of liver damage, correction of hemodynamic disturbances, prolonged survival, and good QoL when performed early in BCS

Similarly good results are obtained with combined SSPCS and CAS in patients with BCS resulting from IVC occlusion.

In contrast, mesoatrial shunt has been discontinued in the authors’ program because of an unacceptable incidence of graft thrombosis and death.

In patients with advanced cirrhosis from long-standing, untreated BCS, LT is the only hope of relief and results in the salvage of some patients.

<table>
<thead>
<tr>
<th>Table 4. LONG-TERM RESULTS OF PORTAL DECOMPRESSION OPERATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Portasystemic encephalopathy (%)</td>
</tr>
<tr>
<td>Employed or housekeeping (%)</td>
</tr>
<tr>
<td>Survival (%)</td>
</tr>
<tr>
<td>30-day</td>
</tr>
<tr>
<td>Current</td>
</tr>
</tbody>
</table>

CAS, cavoatrial shunt; IVC, inferior vena cava; SSPCS, side-to-side portacaval shunt.
# The Evolution of Portal Hypertension Surgery

*Lessons From 1000 Operations and 50 Years’ Experience*

Héctor Orozco, MD; Miguel Angel Mercado, MD


## Table 2. Comparison of the Main Types of Procedures*

<table>
<thead>
<tr>
<th>Variable</th>
<th>DSRS</th>
<th>LDMS</th>
<th>Mesorenal or Mesocaval</th>
<th>Proximal Splenorenal</th>
<th>Portacaval</th>
<th>Sugiura-Futagawa</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>296</td>
<td>37</td>
<td>27</td>
<td>38</td>
<td>103</td>
<td>27 One-stage and 251 abdominal-stage</td>
</tr>
<tr>
<td>Period</td>
<td>5/3†</td>
<td>3</td>
<td>10</td>
<td>14</td>
<td>11</td>
<td>6/2†</td>
</tr>
<tr>
<td>Operative mortality, %</td>
<td>6</td>
<td>15</td>
<td>5</td>
<td>11</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Rebleeding, %</td>
<td>8†</td>
<td>38</td>
<td>40</td>
<td>40</td>
<td>43</td>
<td>4†</td>
</tr>
<tr>
<td>Encephalopathy, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*DSRS indicates distal splenorenal shunt; LDMS, low-diameter mesocaval shunt.
†Past 5 years.
‡Significant difference (P < .05).
Cause of TIPS failure and complications (vecchi) + TIPS
Circulatory changes caused by TIPS and clinical consequences

- TIPS
  - Increase in portal flow
  - Reduction of effective hepatic flow
  - Reduces portal pressure due to the dramatic drop in intrahepatic vascular resistance
  - Reverses the sense of the circulation in the portal venous system within the liver
  - Sinusoidal perfusion highly dependant on the hepatic arterial flow; if uneffective

Progressive Liver Failure

Colombato L, J Clin Gastroenterol 2007;41:S344–S351
The hepatic arterial buffer response (HABR)
Circulatory changes caused by TIPS and clinical consequences

TIPS

- Increase in portal flow
- Reduction of effective hepatic flow
- Reduces portal pressure due to the dramatic drop in intrahepatic vascular resistance
- Reverses the sense of the circulation in the portal venous system within the liver
- Huge escape of portal flow through the stent without interaction at the liver sinusoid level

Portal-Systemic Encephalopathy (PSE)

Colombato L, J Clin Gastroenterol 2007;41:S344–S351
Circulatory changes caused by TIPS and clinical consequences

TIPS

- Increase in portal flow
- Reduction of effective hepatic flow
- Reduces portal pressure due to the dramatic drop in intrahepatic vascular resistance
- High blood flow through the stent with dramatic shift of blood to the systemic circulation

Hemodinamic Changes

1. Increased venous return
2. Normalization of effective arterial blood volume
3. Increased cardiac output
4. Exaggeration of vasodilatation
5. Increase in hyperdynamic circulatory with "normal" portal pressure

Transient rise in right atrial pressure that might potentially worsen an undiagnosed porto-pulmonary hypertension or alternatively it might unmask a subclinical cardiomyopathy, leading to heart failure

Colombato L, J Clin Gastroenterol 2007;41:S344–S351
Complications of TIPS

30-46% Development or worsening in hepatic encephalopathy (HE)

33% Transcapsular puncture → 1-2% Significant intraperitoneal hemorrhage

20% Shunt malpositioning

10% Deterioration of hepatic function

Rare: Clinically significant hemobilia
Shunt migration
Hepatorenal syndrome

Fidelman et al, AJR 2012; 199:746–755
Colombato L, J Clin Gastroenterol 2007;41:S344–S351
Causes of TIPS failure → RECURRENCE OF PORTAL HYPERTENSION

1. Intimal hyperplasia
2. Thrombotic occlusion
3. Hepatic venous end shunt stenosis
4. Portal venous end shunt stenosis
5. Abnormal angulation
6. Occult portosystemic pressure gradient elevation
7. Flow-sumping

Stenosis (up to 70%) & Occlusion

Fidelman et al, AJR 2012; 199:746–755
**TIPS Maintenance**

Most hepatologists order routine TIPS surveillance tests at regular intervals using ultrasound with Doppler in asymptomatic patients.

**US-Doppler marks of TIPS dysfunction:**

Alterations in shunt velocities:
- 250 cm/s or higher
- 50 cm/s or less

are associated with > 90% sensitivity and specificity for shunt dysfunction.
Patients with a suspected TIPS dysfunction should undergo:

- TIPS venography
- Replacement of bare stent with covered stent
- Balloon angioplasty within the stent
- Placement of additional stents in patients to extend cranial or caudal length of the stent

HE refractory to medical management and progressive hepatic dysfunction might require endovascular shunt reduction

Need for repeated revisions: Are TIPS cost-effective?
Contraindications to TIPS placement

### TABLE 4: Contraindications to Placement of a Transjugular Intrahepatic Portosystemic Shunt

<table>
<thead>
<tr>
<th>Absolute</th>
<th>Relative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary prevention of variceal bleeding</td>
<td>Hepatocellular carcinoma, especially central</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>Obstruction of all hepatic veins</td>
</tr>
<tr>
<td>Severe tricuspid regurgitation</td>
<td>Portal vein thrombosis</td>
</tr>
<tr>
<td>Severe pulmonary hypertension</td>
<td>Moderate pulmonary hypertension</td>
</tr>
<tr>
<td><strong>Multiple hepatic cysts</strong></td>
<td>Severe coagulopathy (international normalized ratio &gt; 5)</td>
</tr>
<tr>
<td>Uncontrolled systemic infection or sepsis</td>
<td>Thrombocytopenia of &lt; 20,000 cells/cm³</td>
</tr>
<tr>
<td>Unrelieved biliary obstruction</td>
<td>Hepatic encephalopathy</td>
</tr>
</tbody>
</table>

Contraindications of TIPS placement are not necessary applicable to surgical shunts:

Could indication to PSS be extended over tips indications?
Uncovering the truth about covered stents: is there a difference between covered versus uncovered stents with transjugular intrahepatic portosystemic shunts?

246 Patients with PH undergoing TIPS from 2001 to 2010

70 → uncovered stents
176 → covered stents

Patients who received uncovered stents had more severely impaired liver function (41% were Child class C cirrhotics).

Covered stents may improve patency but do not mitigate postshunt hepatic dysfunction and do not improve survival

Follow-up

<table>
<thead>
<tr>
<th></th>
<th>Covered</th>
<th>Uncovered</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reintervention for stenosis (P = 0.01)</td>
<td>33%</td>
<td>19%</td>
</tr>
<tr>
<td>Shunt dysfunction (P = 0.05)</td>
<td>57%</td>
<td>21%</td>
</tr>
<tr>
<td>Deterioration of hepatic function (P = 0.32)</td>
<td>31%</td>
<td>30%</td>
</tr>
<tr>
<td>Survival (P = 0.55)</td>
<td>31 months</td>
<td>33 months</td>
</tr>
</tbody>
</table>

To determine the long-term cost-effectiveness of TIPS vs. Surgical PSS

The main outcome was dollars per life-year saved:

- **Average cost per life year saved:**
  - TIPS: $17,771 (SD = 471)
  - PSS: $21,438 (SD = 308)

- **Average life expectancy:**
  - TIPS: 5.0 years
  - PSS: 7.0 years

This yielded an incremental cost-effectiveness rate for PSS of $3,299 per life year saved.

Compared with TIPS, PSS resulted in improved survival with minimal increase in cost.

Therefore, given the low incremental cost of PC, it should be adopted as a cost-effective strategy in managing this patient population.
Clinical Science

Outcomes after transjugular intrahepatic portosystemic stent shunt: a “bridge” to nowhere

Paul G. Toomey, M.D.\textsuperscript{a,c}, Sharona B. Ross, M.D.\textsuperscript{a,c}, Farhaad C. Golkar, M.D.\textsuperscript{b,d}, Jonathan M. Hernandez, M.D.\textsuperscript{a}, Whalen C. Clark, M.D.\textsuperscript{a}, Kenneth Luberice, B.S.\textsuperscript{b,c}, Angel E. Alsina, M.D.\textsuperscript{a,b}, Alexander S. Roseurgy, M.D.\textsuperscript{b,c,x}
Who should receive TIPS?

Patients:

→ who are imminently going to be transplanted (within 6 months)
→ with high cardiopulmonary risk for abdominal surgery (eg, aortic stenosis and mitral regurgitation)
→ with a “hostile abdomen” (eg, multiple previous celiotomies)
→ extremely obese

Other than this select group, patients should not undergo TIPS without any expectation other than a short survival complicated by shunt surveillance and shunt failure

For patients with poor hepatic function (eg, CPT-C) resource allocation is promoted by surgical shunting

The concept of operative shunting needs to be reconsidered and revisited
Surgical and Endovascular Treatment of Severe Complications Secondary to Noncirrhotic Portal Hypertension: Experience of 56 Cases

PSS:
- Shunt patency: 100%
- Rebleeding: 0%

Esophagogastric devascularization:
- 2/3 was converted to mesocaval shunt due to recurrent variceal bleeding (at 8, 13, and 24 months)
- 1/3 died before redo operation

Thrombolysis:
- ¾ survived without complications
- ¼ death for small bowel infarction due to recurrent thrombosis at 40 days form procedure

Platelet counts from 43x10⁹/L to 239x10⁹/L 2 within 2 weeks
Ascites disappeared in 30/31 within 2 months

No post-operative encephalopathy
Peri-operative 30-day mortality. 0%

PSS can be employed to treat bleeding esophagogastric varices and severe hypersplenism in patients with NCPH

PSE is less of a concern in NCPH patients with normal liver function

Endovascular thrombolysis is a useful alternative treatment for acute portal and/or mesenteric venous thrombosis

Surgical management of portal biliopathy: Summary of case-series and case-reposts

<table>
<thead>
<tr>
<th>Ref.</th>
<th>No. of patients</th>
<th>Biliary abnormalities</th>
<th>First treatment</th>
<th>Follow-up</th>
<th>Further treatments</th>
<th>Complications/outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chaudhary et al[6], 1998</td>
<td>9 symptomatic</td>
<td>Stenosis: 2 CBD stones: 2</td>
<td>BA 2</td>
<td>9 pts</td>
<td>BA 2</td>
<td>Death 1</td>
</tr>
<tr>
<td>Condat et al[9], 2003</td>
<td>7 symptomatic</td>
<td>Cholecystitis/right hypochondral pain 4 Cholangitis 7 Stenosis 2</td>
<td>Cholecystostomy + ERCP 1 Stent 1</td>
<td>4-25 mo</td>
<td>Stent 1 ES + SE 2</td>
<td>Resolution 7</td>
</tr>
<tr>
<td>Gauthier-Villars et al[10], 2005</td>
<td>8 symptomatic (pediatric)</td>
<td>Biliarydilation 8 A: Stenosis 5 B: CBD stones 3 C: Stenosis + CBD stones 5</td>
<td>A: PSS 4; BA 1 B: ERCP 2; PSS + BA 1</td>
<td>4.5-15 yr</td>
<td>C: Multiple ERCP 2; BA 1; Splenectomy + BA 1</td>
<td>Haemobilia 1</td>
</tr>
<tr>
<td>Khare et al[11], 2005</td>
<td>13 symptomatic</td>
<td>Biliarydilation 8 A: Stenosis 5 B: CBD stones 3 C: Stenosis + CBD stones 5</td>
<td>A: PSS 4; BA 1 B: ERCP 2; PSS + BA 1</td>
<td>4.5-15 yr</td>
<td>C: Multiple ERCP 2; BA 1; Splenectomy + BA 1</td>
<td>Complete resolution 7</td>
</tr>
<tr>
<td>Vibert et al[12], 2007</td>
<td>19 symptomatic</td>
<td>IE biliary dilation 9 IE stones 7 CBD stones 4</td>
<td>PSS group: PTBD 1 SRS 10</td>
<td>19 pts</td>
<td>BA 5 NPSS group</td>
<td>Partial resolution 1</td>
</tr>
<tr>
<td>D' Souza et al[13], 2009</td>
<td>1 symptomatic CBD stenosis + GB stones Mirizzi's syndrome</td>
<td>Pre-surgery stent→PSS + BA (single stage)</td>
<td></td>
<td>18 mo</td>
<td>Multiple stent exchange in pts initially treated with stent</td>
<td>Cholangitis in 2 pts treated with stent</td>
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<tr>
<td>Agarwal et al[14], 2011</td>
<td>39 symptomatic</td>
<td>Stenosis 15 CBD stones 7 GB stones 12</td>
<td>ES + stent 2 ES + SE 1 PTBD 6</td>
<td>37 pts</td>
<td>BA 12</td>
<td>Resolution 35</td>
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<tr>
<td>Chattopadhyay et al[15], 2012</td>
<td>24 asymptomatic CBD stenosis 3 Multiple stenosis 5</td>
<td>ERCP pre-surgery 12</td>
<td></td>
<td>19 mo</td>
<td>Multiple ES + stent 5</td>
<td>Resolution 38</td>
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<tr>
<td>Suárez et al[16], 2013 Bhatta et al[17], 2014 Liu et al[18], 2015</td>
<td>3 symptomatic GB stones Stenosis 6 Dilations 6</td>
<td>UDCA 1 BA 1 Cholecistectomy</td>
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Franceschet I et al, World J Gastroenterol 2016 December 7; 22(45): 9909-9920
Causes of NCPH
According to blood flow site resistance

<table>
<thead>
<tr>
<th>Pre-hepatic</th>
</tr>
</thead>
<tbody>
<tr>
<td>FHVP normal, RAP normal, WHVP normal, HVPG normal, PVP high, ISP high</td>
</tr>
<tr>
<td>Extrahepatic portal vein obstruction (EHPVO)</td>
</tr>
<tr>
<td>Portal vein thrombosis</td>
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<tr>
<td>Splenic vein thrombosis</td>
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<tr>
<td>Splanchnic arteriovenous fistula</td>
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<tr>
<td>Massive splenomegaly</td>
</tr>
<tr>
<td>Infiltrative diseases-Lymphoma, myeloproliferative disorders</td>
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<tr>
<td>Storage diseases-Gaucher’s disease</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Post-hepatic</th>
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</thead>
<tbody>
<tr>
<td>FHVP high, RAP normal or high, WHVP high, HVPG normal or high, PVP high, ISP high**</td>
</tr>
<tr>
<td>Inferior vena cava obstruction-web, thrombosis, tumour, enlarged caudate lobe</td>
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<tr>
<td>Constrictive pericarditis</td>
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<tr>
<td>Tricuspid regurgitation</td>
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<tr>
<td>Severe right-sided heart failure</td>
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<tr>
<td>Restrictive cardiomyopathy</td>
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</table>
# Causes of NCPH
According to blood flow site resistance

<table>
<thead>
<tr>
<th></th>
<th>Pre-sinusoidal</th>
<th>Sinusoidal</th>
<th>Post-sinusoidal</th>
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<tbody>
<tr>
<td><strong>Hepatic</strong></td>
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<tr>
<td>FHVP normal</td>
<td>Developmental abnormalities</td>
<td>Sinusoidal fibrosis</td>
<td>Venoocclusive disease</td>
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<tr>
<td>RAP normal</td>
<td>Adult polycystic disease</td>
<td>Alcoholic hepatitis</td>
<td>Hepatic irradiation</td>
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<tr>
<td>WHVP high</td>
<td>Hereditary hemorrhagic disease</td>
<td>Drugs (methotrexate, amiodarone)</td>
<td>Toxins-Pyrrolizidine alkaloids</td>
</tr>
<tr>
<td>HVPG normal or high</td>
<td>Arteriovenous fistulas</td>
<td>Toxins (vinyl chloride, copper)</td>
<td>Drugs-Gentuzumab, ozogamicin,</td>
</tr>
<tr>
<td>PVP high</td>
<td>Congenital hepatic fibrosis</td>
<td>Metabolic (NASH, Gaucher's disease)</td>
<td>actinomycin D, dacarbazine, cytosine</td>
</tr>
<tr>
<td>ISP high*</td>
<td>Biliary diseases</td>
<td>Inflammatory (viral hepatitis, Q fever,</td>
<td>arabinoside, mithramycin, 6-thioguanine,</td>
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<td></td>
<td>Primary biliary cirrhosis</td>
<td>healed cytomegalovirus, secondary</td>
<td>azathioprine, busulfan plus</td>
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<td></td>
<td>Sclerosing cholangitis</td>
<td>syphilis)</td>
<td>cyclophosphamide</td>
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<td>Autoimmune</td>
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<td>Sinusoidal collapse</td>
<td>Phlebosclerosis of hepatic veins</td>
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<td>cholangiopathy</td>
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<tr>
<td>Toxic-Vinyl</td>
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<td>Acute necro-inflammatory diseases</td>
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<td>chloride</td>
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<td>Neoplastic</td>
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<td>Sinusoidal defenestration</td>
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<tr>
<td>occlusion of portal vein</td>
<td>Lymphoma</td>
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<td>Epithelioid hemangioendothelioma</td>
<td>Sinusoidal infiltration</td>
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<td>Epithelial malignancies</td>
<td>Mastocytosis</td>
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<td>Chronic lymphocytic leukemia</td>
<td>Agnogenic myeloid metaplasia</td>
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<td>Granulomatous lesions</td>
<td>Gaucher's disease</td>
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<td>Schistosomiasis</td>
<td>Amyloidosis</td>
<td>Granulomatous phlebitis</td>
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<td>Mineral oil granuloma</td>
<td>Sinusoidal compression</td>
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<td>Sarcoïdosis</td>
<td>By enlarged Kupffer cells (Gaucher's</td>
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<td>Hepatoporal sclerosis</td>
<td>disease, visceral Leishmaniasis)</td>
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<td>Peliosis hepatitis</td>
<td>By enlarged fat-laden hepatocytes</td>
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<td></td>
<td>Partial nodular transformation</td>
<td>(Alcoholic hepatitis, AFLP)</td>
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<td></td>
<td>Noncirrhotic portal fibrosis (NCPF)</td>
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<td></td>
<td>Idiopathic portal hypertension (IPH)</td>
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Khanna R et al, J Hepatol 2014 vol. 60; 421–441
Lavori dimenticati
Cose vecchie utili: pelli di foca
### Table 3. Diagnostic criteria of idiopathic non-cirrhotic portal hypertension.*

1) Clinical signs of portal hypertension (any one of the following**)
   - Splenomegaly/hypersplenism
   - Esophageal varices
   - Ascites (non-malignant)
   - Minimally increased hepatic venous pressure gradient
   - Portovenous collaterals

2) Exclusion of cirrhosis on liver biopsy

3) Exclusion of chronic liver disease causing cirrhosis or non-cirrhotic portal hypertension†
   - Chronic viral hepatitis B/C
   - Non-alcoholic steatohepatitis/alcoholic steatohepatitis
   - Autoimmune hepatitis
   - Hereditary hemochromatosis
   - Wilson's disease
   - Primary biliary cirrhosis

4) Exclusion of conditions causing non-cirrhotic portal hypertension
   - Congenital liver fibrosis
   - Sarcoidosis
   - Schistosomiasis

5) Patent portal and hepatic veins (doppler ultrasound or computed tomography scanning)

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*All criteria must be fulfilled in order to diagnose NCPH. **Splenomegaly must be accompanied by additional signs of portal hypertension in order to fulfil this criterion. †Chronic liver disease must be excluded since severe fibrosis might be underaged on liver biopsy.