Trombosis de la Vena Porta en Cirróticos y no Cirróticos: Manejo

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Portal Vein Thrombosis

Diagnosis of PVT requires to define.

- Partial/Occlusive (% of lumen occluded/or of patency?)
- Segments of the Portal Venous Axis affected (branches/trunk/splenics/mesenteric?)
- Acute/Chronic?
- Signs of Intestinal Ischemia?

• Healthy or Disease Liver (Cirrhosis/IPH/other)

US-Doppler the first choice technique for thrombosis detection. Confirm and evaluate extension with Angio-CT or Angio-MRI
PVT on a Healthy Liver. Etiology

<table>
<thead>
<tr>
<th>Acquired or Inherited Prothrombotic Dis.</th>
<th>40-50%</th>
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</thead>
<tbody>
<tr>
<td>- Myeloproliferative Syndromes</td>
<td></td>
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<tr>
<td>- Prothrombin gen mutation</td>
<td></td>
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<tr>
<td>- Others</td>
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</table>

**Local Factor:** Surgery, abd. inflammation… 20-30%

**Idiopathic** 20-30%

- >50% more than one prothrombotic disorder
- 36% of those with a local factor, also had a general prothrombotic disorder

Portal Hypertension leads to Splenomegaly with Hypersplenism and Plasma Volume Expansion with Hemodilution

These alterations mask increases in blood cell parameters. JAK2; Calreticulin!!

Plessier for the Envie Group. Hepatology 2010
Risk factors for developing PVT on Cirrhosis

- Severity of Liver Disease (Child)
- Reduction in Portal Blood Flow Velocity
- No clear etiological role for inherited or acquired prothrombotic states. May influence Rx decisions?
PVT in Healthy Liver

Acute PVT

- Abd. Pain/Intestinal Isch.
  - Infarction

Chronic PVT/Portal Cavernoma

- Variceal Bleeding
- Recurrent Thrombosis
- Portal Colangiopathy
  - Others

Aim of Rx in Acute PVT:

- Prevent Ischemic Complications
- Prevent Progression to Chronic
Treatments Used for Acute Thrombosis of the Portal Venous System

- Anticoagulation
- Thrombolysis / Thrombectomy

No comparative studies
Recanalization rate in anticoagulated patients with Acute Portal, Superior Mesenteric, or Splenic Vein Thrombosis

Portal Venous System completely patent in 20% of patients

Plessier for the Envie Group. Hepatology 2009
Low number of adverse events

- 9 bleeding (5 GI; 3 Severe: No mortality)
- 2 death (1 Late malignancy and 1 sepsis)
- 2 Intestinal Infarction, limited intestinal resection, both pts survived
Thrombolytic Therapy in Acute thrombosis of the PV System
Rate of Recanalization and complications

- Almost 100% success of thrombolytic therapy with a low incidence of complications in reported cases. Potential publication bias.

![Recanalization](image1)

![Complications](image2)

Hollingshead et al. JVIR 2005 (n=20) | Smalberg et al. Thromb Haemost 2008 (n=12)
Chronic PVT Complications. Esophageal Varices

After non recanalized acute PVT

- Perform early endoscopy (2-3 m) for EV screening.
- If negative, and no complete recanalization, repeat at 9-12 months.

Up to 75% of patients have EV at the endoscopy performed at the diagnosis of chronic PVT.

Endoscopy at diagnosis of Chronic PVT is mandatory

Rx Strategy: As in patients with Cirrhosis
Recurrent Thrombosis in pts with NCNT-PVT

- More common than suspected, but frequently asymptomatic and only recognized if intentionally investigated
- Rethrombosis may deteriorate outcome (EV, Colangiopathy)
- Different risk according with underlying etiology.

Anticoagulation in Chronic PVT if:

- Existence of an underlying prothrombotic disorders
- Previous thrombosis of other vascular territories
- Rethrombosis/thrombosis progression

Prevents recurrent thrombosis without * or with **more risk of GI bleeding but without increasing the severity of bleeding when it occurs

Anticoagulation must always be delayed until treatment to prevent variceal bleeding has been initiated
Recurrent Thrombosis on the PV system according to etiology in a cohort of 108 Pts with Chronic PVT

Log-rank test, p=0.382

Number at risk

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>12</th>
<th>24</th>
<th>36</th>
<th>48</th>
<th>60</th>
<th>72</th>
<th>84</th>
<th>96</th>
<th>108</th>
<th>120</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prothrombotic</td>
<td>10</td>
<td>10</td>
<td>8</td>
<td>7</td>
<td>6</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Mieloproliferative</td>
<td>29</td>
<td>27</td>
<td>23</td>
<td>21</td>
<td>15</td>
<td>13</td>
<td>12</td>
<td>11</td>
<td>7</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>Idiop. or Local factor</td>
<td>69</td>
<td>64</td>
<td>54</td>
<td>51</td>
<td>41</td>
<td>37</td>
<td>31</td>
<td>26</td>
<td>19</td>
<td>15</td>
<td>14</td>
</tr>
</tbody>
</table>
Recurrent Thrombosis in patients with Idiopathic or Underlying Local Factors receiving or not ACO

Log-rank test, p=0.168

Is there a group of patients with Idiopathic thrombosis or secondary to local factors that need to be also treated with long-term anticoagulation?
Patients With Non-Cirrhotic Non-Malignant Chronic Portal Vein Thrombosis had a Good Prognosis

> 85% Survival at 5 y

Rajani et al. Aliment Pharmacol Ther 2010; 32: 1154-1162
PVT in Cirrhosis, Important health problem?

1 y median incidence 13%
(range: 4.6-19%)
In more than 2/3 detected at a routine screening HCC imaging study

Reported Rates of Spontaneous recanalization or improvement (0-47%) and of progression (7.2-71%) highly heterogeneous.

Natural History still no defined. May be we need a longer follow-up to determine the real rate of PVT Improvement or progression.
PVT in Cirrhosis. Clinical Impact?

• A large prospective study of cirrhotic pts without PVT shows that risk factors associated to liver decompensation are similar to those associated to PVT development.

• However, PVT development did not increase the rate of liver decompensation.

(Nery et al. Hepatology 2015)

Most PVTs in the study partial. Relative Short follow-up!
In patients with cirrhosis and potential OLT candidates preventing the development of severe forms of PVT (grade 3 and 4) impact outcome.

Yerdel et al. Transplantation 2000
PVT in Cirrhosis. Anticoagulation Efficacy

- Most studies retrospective
- Small Sample Size (19-55 patients)
- Different Anticoagulants (2 LMWH; 2 LMWH then VKA; 1 VKA)
- Improvement (42-84%)
  - Complete recanalization (36-75%)
  - Partial recanalization (0-43%)
- Stable (17-40%)
- Progression despite ACO (0-15%)
## Anticoagulation in PVT in Cirrhosis. Complications

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Francoz /2005 (n=19)</td>
<td>LMWH/VKA</td>
<td>1 post-EBL Bleeding</td>
</tr>
<tr>
<td>Amitrano /2010 (n=28)</td>
<td>LMWH</td>
<td>2 PHG anemia</td>
</tr>
<tr>
<td>Senzolo /2012 (n=33)</td>
<td>LMWH</td>
<td>3 Non-VB (1 non fatal cerebral)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 VB</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 Heparin Induced Thrombopenenia</td>
</tr>
<tr>
<td>Delgado /2012 (n=55)</td>
<td>LMWH-LMWH/VKA</td>
<td>5 Non-VB</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6 VB</td>
</tr>
<tr>
<td>Werner /2013 (n=28)</td>
<td>VKA</td>
<td>1 Non-VB</td>
</tr>
</tbody>
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More bleeding with VKAs if platelet count below 50,000? More data needed

**No Mortality related to Anticoagulation**
What should be done if recanalization is achieved?

- Pathophysiological mechanisms leading to the development of thrombosis remain

- Amitrano et al. 2010.
  
  Three of 11 (27%) patients who stopped anticoagulation after achieving recanalization showed rethrombosis at 1, 4, and 24 months

- Delgado et al. 2012.
  
  5 of 13 pts (38.5%) had rethrombosis a median of 1.3 months after stopping anticoagulation.

Long-Term anticoagulation?
Treatment of PVT in Cirrhosis. Points to Consider

- Actual or Potential OLT Candidate
- PVT Extension (partial or occlusive)
- Adequate portal vessels for OLT
- Thrombophilia assessment

Develop specific guidelines for your Center that will allow evaluation of results
**PVT in Cirrhosis. Barcelona Algorithm**

**PVT Extension**: Extense Thrombosis (>50% thrombosis of any of the 3 major PV vessels; 25-50% of 2 vessels: more than 2)

- **YES**
  - Follow-up US (1 month) + **Thrombophilia Assessment**
  - **Thrombophilia (High-risk +)** or **Thrombosis Progression to extense PVT**
    - **YES**
    - Follow-up Imaging Study every 3 m during one year then every 6 m
      - **Thrombosis Progression to extense PVT**
    - **NO**
      - **NO**

- **NO**
  - Follow-up Imaging Study every 3 m during one year then every 6 m
If feasible, Stop ACO except if high-risk trombofilia.

No OLT Candidacy

US 1 m

Adequate Vessels for OLT

Consider TIPS ± thrombolisi

If feasible, Stop ACO except if high-risk trombofilia

ACO 6-12 m

Adequate Vessels for OLT?

YES

Long-Life ACO

No

Stop ACO except if High-Risk Trombofilia

Consider long-life ACO if recurrent Thrombosis

ACO 6-12 m

Adequate Vessels for OLT?

YES

NO
The Barcelona Portal Hypertension Team

Vascular liver diseases collaborative group

Barcelona Hepatic Hemodynamics Laboratory