Complete hepatic surgical resection of primary or secondary liver malignancies, remains the first choice of a curative treatment and the only chance of long term survival, for the patient.

The major risk of these extended resections is the liver post-operative failure. A minimal volume of liver (Future Liver Remnant = FLR) is necessary before an enlarged hepatectomy.
Pre-operative portal vein embolization (PVE) is a venous portal occlusion, selective, performed through a percutaneous approach. The PVE induce a hypertrophy of the contralateral liver, indicated in case or future liver remnants (FLR), estimated insufficient. The rate of minimal FLR is function of the liver itself:

- FLR < 30% for normal liver,
- FLR < 40 % for fibrosis liver,
- FLR < 20% for normal liver,
- FLR < 30 % if neo-adjuvant chemotherapy
- FLR > 40 % in case of cirrhosis.
A comprehensive knowledge of functional liver anatomy is imperative for performing PVE.
The most widely classification system was proposed in 1957 by Couinaud.
The liver is divided in two hemi livers (left and right, separated by the main portal fissure) in 8 segments.
Hepatic segmentation is based on the distribution of the portal pedicles and the location of the hepatic veins.
Normal Anatomy

Extended right hepatectomy
Right trisegmentectomy

Right hepatectomy

Left hepatectomy

Extended left hepatectomy
Left trisegmentectomy
Portal Vein Variants
Indications

Decision to perform PVE:
• Ratio of FLR to total estimated liver volume (TELV), should be calculated.
• Cases (patients) need to be categorized into those with and those without underlying liver disease = this factor will determinate how much FLR is needed to reduce post-operative morbidity and mortality.

A FLR/TELV ratio, at least 25 % is recommended in patients with normal livers.

A FLR/TELV ratio, at least 40 % in patients with compromised liver (chronic liver disease, chemotherapy).
When FLR/TELV ratio are below these levels, PVE may be performed in an attempt to increase FLR volume.
Contra Indications

Patients with metastatic diseases, such distant metastases or periportal lymphadenopathy are not candidates for PVE.

Other « relative » contraindications:

- uncorrectable coagulopathy,
- tumor invasion of the portal vein,
- biliary dilatations (endoscopic drainage)
- portal hypertension
- renal failure (dialysis)
- portal tumor vein invasion.
Techniques

Before:

Complete patient history, physical examination.

Laboratory studies (blood cell count, prothrombin time, liver function tests, blood urea, creatinine) are essential to control prior to PVE.

CT and MRI scanning: « fundamental » radiological investigation prior to PVE.
PVE Techniques

General anesthesia is requested generally.

Portal vein access: under ultrasound guidance to puncture a peripheral branch:

- contralateral approach (left portal branch and embolization of the right portal branch).
- ipsilateral approach (puncture of the right portal branch, to embolize right portal branches).

Five french materials: introductory sheath, catheter.

First venous angiography: the catheter is placed at the splenomesenteric confluence:

- to visualize portal anatomy, including variations.
- to localize segment IV branches.
Aim of PVE: complete obstruction of the targeted branches and redistribution of flow to the FLR branches only.

Embolization of segment IV branches is recommended in patients with tumors, who are undergoing extended right hepatectomy.
Final portography is mandatory to verify this objective.

Sheath ablation and embolization of the intra-liver parenchyma with Gelitaspon® (resorbables particles).
Measurement of the time of the procedure and the degree of Rx irradiation (scopy-graphy).
### Embolic Agents Choice

Influence of embolic agent on the hypertrophy response PVA, polyvinyl alcohol, Glue.

<table>
<thead>
<tr>
<th>Embolic agent</th>
<th>Authors</th>
<th>No. of patients</th>
<th>Increase FRL (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gelatin sponge</td>
<td>Fujii et al. (24)</td>
<td>30</td>
<td>17.8</td>
</tr>
<tr>
<td></td>
<td>Kusaka et al. (25)</td>
<td>18</td>
<td>21.2</td>
</tr>
<tr>
<td></td>
<td>Kakizawa et al. (26)</td>
<td>14</td>
<td>23.8</td>
</tr>
<tr>
<td></td>
<td>Nanashima et al. (27)</td>
<td>30</td>
<td>29.4</td>
</tr>
<tr>
<td>PVA + coils/plugs</td>
<td>Covey et al. (28)</td>
<td>100</td>
<td>24.3</td>
</tr>
<tr>
<td></td>
<td>van den Esschert JW et al. (29)</td>
<td>10</td>
<td>26.1</td>
</tr>
<tr>
<td></td>
<td>Libicher et al. (30)</td>
<td>10</td>
<td>26.4</td>
</tr>
<tr>
<td>N-butyl cyanoacrylate</td>
<td>De Baere et al. (31)</td>
<td>107</td>
<td>57.8</td>
</tr>
<tr>
<td></td>
<td>Giraudo et al. (32)</td>
<td>146</td>
<td>41.7</td>
</tr>
<tr>
<td></td>
<td>Elias et al. (33)</td>
<td>68</td>
<td>59.1</td>
</tr>
<tr>
<td></td>
<td>Broering et al. (1)</td>
<td>17</td>
<td>69.4</td>
</tr>
<tr>
<td>Fibrin glue</td>
<td>Nagino et al. (34)</td>
<td>105</td>
<td>27.4</td>
</tr>
<tr>
<td></td>
<td>Liem et al. (35)</td>
<td>15</td>
<td>31.4</td>
</tr>
</tbody>
</table>
Embolic Agents Choice

Recommended products include the following:

Glue mixture:
  - n-butyl 2 – cyanoacrylate (NBCA, Histoacryl® (with Lipiodol®) (Braun, Germany).
  - Glubran2® (GEM, Italy, with Lipiodol®).

Onyx mixture:
  - glue without mixture, before DMSO® (Medtronic, USA). Advantages: slow injections, no risk of reflux.

Advantages: Glue allows fast procedure in comparison with other embolic agents.
Woman, 56 years old.

Cystic disease with soft component within the hilum (Caroli Syndrome).
Woman, 35 years old.

Hepato carcinoma of the right liver.
Healthy liver
Right portal vein branches embolization.
Control: only the left lobe is present
Post Procedural Monitoring

Evaluation for signs of post-embolization syndrome:
- review of patients symptoms, clinical signs.
- laboratory data.

Patients are discharged when they are clinically stable, without complaints, usually the next day.

Outcomes:
Technical success rate is close to 100 %.
Resection rate after 4-6 weeks is approximately 85 %
(difference: tumor progression, metastases).
## Potential complications after PVE

<table>
<thead>
<tr>
<th>Type of complications</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Minor complications</strong></td>
<td></td>
</tr>
<tr>
<td>Fever</td>
<td>36.9</td>
</tr>
<tr>
<td>Elevation of transaminase</td>
<td>34.8</td>
</tr>
<tr>
<td>Abdominal discomfort/pain</td>
<td>22.9</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>2</td>
</tr>
<tr>
<td>Ileus</td>
<td>1.2</td>
</tr>
<tr>
<td><strong>Major complications</strong></td>
<td></td>
</tr>
<tr>
<td>Portal thrombosis</td>
<td>0.8</td>
</tr>
<tr>
<td>Embolization of nontarget vessels</td>
<td>0.6</td>
</tr>
<tr>
<td>Liver hematoma</td>
<td>0.4</td>
</tr>
<tr>
<td>Infection/abscess</td>
<td>0.4</td>
</tr>
<tr>
<td>Intra-abdominal bile leakage</td>
<td>0.3</td>
</tr>
</tbody>
</table>
Hypertrophic Response Volumetry

CT, with volumetric is the cornerstone for planning surgical resection. There are different methods of calculating liver volumes making difficult comparisons of results obtained at different institutions.

In patients with normal liver and liver metastases and/or hepatic carcinoma, the increase of the FLR ratio is between 8% and 25%, regeneration is always observed after PVE.

In cirrhotic-fibrosis patients, PVE fails to induce left-lobe hypertrophy in 20% of cases (increased rate of FLR ratio in this population is lower, 6% - 20%).
Volumetry

Myrian soft.

- Semi-automatic hepatic parenchyma segmentations virtual right assisted hepatectomy.
- Systematic volumetries of total liver, right and left.
<table>
<thead>
<tr>
<th></th>
<th>Hypertrophie du foie gauche</th>
<th>Gain de FFR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foie sain</td>
<td>58%</td>
<td>18%</td>
</tr>
<tr>
<td>Chimiothérapie</td>
<td>30%</td>
<td>13%</td>
</tr>
<tr>
<td>Fibrose F1-F2</td>
<td>21%</td>
<td>5%</td>
</tr>
<tr>
<td>Cirrhose F3-F4</td>
<td>15%</td>
<td>6%</td>
</tr>
</tbody>
</table>

**Volumetry**
<table>
<thead>
<tr>
<th>Authors</th>
<th>Embolization Agent</th>
<th>Patient Number</th>
<th>Hypertrophy FLR</th>
<th>FLR gain</th>
</tr>
</thead>
<tbody>
<tr>
<td>De Baere and al, 1996</td>
<td>cyanoacrylate</td>
<td>24</td>
<td>70.4%</td>
<td>13%</td>
</tr>
<tr>
<td>Covey and al, 2005</td>
<td>PVA</td>
<td>39</td>
<td>24.3%</td>
<td>9%</td>
</tr>
<tr>
<td>Tsuda and al, 2006</td>
<td>Coils and resorbables particles</td>
<td>22</td>
<td>8.2%</td>
<td>8.5%</td>
</tr>
<tr>
<td>Descat and al, 2006</td>
<td>AVP I</td>
<td>7</td>
<td>18%</td>
<td>8%</td>
</tr>
<tr>
<td>Yoo and al, 2009</td>
<td>AVP II et particules résorbables</td>
<td>41</td>
<td>25.4%</td>
<td>7%</td>
</tr>
<tr>
<td>Personnal series</td>
<td>ONYX®, Glubran®</td>
<td>15/year</td>
<td>28%</td>
<td>10%</td>
</tr>
</tbody>
</table>
Complications

PVE: considerably less toxic than arterial embolization.

Signs and symptoms:

- post-embolization syndrome, nausea, vomiting.
- Fever and pain, infrequent.
- Liver function changes.

It is essential to avoid the reflux of embolizing material into the portal venous branches of the remnant liver.
49 years old woman.
Hilum cholangio-carcinoma (Klatskin).
Right portal vein branches embolization.
Abdominal catheter for collection drainage (pancreatitis after biliary tract catheterism)
Post operative CT control.
Biloma diagnosis and immediate percutaneous drainage
Questions Regarding PVE Issues (1)

- The purpose of PVE is to increase the hepatic functional reserve of FLR, as well as its volume.

- There are four potential issues facing PVE:
  - PVE stimulates the growth of hepatic tumor,
  - PVE fail to increase the volume of FLR in some patients (fibrotic, cirrhotic liver).
  - PVE safe in patients with high-grade varices?
  - The mechanisms of fast tumor growth after PVE are poorly understood:
The mechanisms of fast tumor growth after PVE are poorly understood:

– Hokudo: In 18 patients with colorectal metastases, he found a increased tumor Ki-67 labeling index in the metastases group with PVE, compared to hepatic metastases without PVE.

– Barbara: he notes a significant increase in hepatic tumor volume from colorectal carcinoma after PVE, while hepatic tumor volume from carcinoid tumor was unchanged.

– Other factor (?): to stimulate tumor growth after PVE is increased hepatic arterial blood flow in embolized liver after PVE (intrahepatic metastases depend on arterial blood supply).
Questions Regarding PVE Issues (3)

• Exact role of Butyrate apoptosis and antiangiogenic effects on colon cancer cells, but arterial flow is increased in hepatic lobe after PVE.
  Idea: to combine with TACE, to prevent Tumor growth in treated right lobe, and to accelerate the hypertrophy of the FLR (INABA, SUGAWARA).

• PVE performed before to an extended right hepatectomy: embolization (complementary) of the IV segment.
  – Accelerated tumor growth has been reported with incomplete embolization (ELIAS).
  – Segment IV embolization may contribute to better hypertrophy of segments I, II, III before extended right hepatectomy.
Discussion

• No procedural failure.
• Anatomical radio analysis of the portal vein distribution is fundamental
• Generally, left portal vein approach (US)
• No true idea of the cost!
• Glue is the best embolization agent.
• Mean time: one hour an a half
• Mean time hospitalization: 3-4 days
• Surgery: between 4-6 weeks, after PVE
• For some authors:
  – temporary occlusion of the sus hepatic vein?
  – TACE just before PVE?
Conclusion

Pre-operative PVE is an affective method to increase FRL volume with a high technical and clinical success rate.

The complication rate is low, but local tumor progression after PVE is a imminent cause of unresectability.

Pre-existing liver damage due to cirrhosis seems to have a negative effect on the hypertrophy responses.

The use of glue (n-butyl cyanoacrylate, Onyx®) may result in a greater hypertrophy response, compared with other embolization materials used.
Bibliography II

Bibliography III


