PERCUTANEOUS INTRAHEPATIC SPLIT BY MICROWAVE ABLATION (PISA)

ALESSANDRO LUNARDI, MD
AUGMENTED PORTAL VEIN EMBOLISATION TECHNIQUES

aPVE
Disclosure

Speaker: Alessandro Lunardi

I do not have any potential conflict of interest
Augmented Portal Vein Embolisation Techniques (APVE)

Portal vein embolization (PVE) is a technique used before hepatectomy to increase the size of liver segments that will remain after surgery. This therapy redirects portal blood to segments of the future liver remnants (FLR), resulting in hypertrophy.

Barcellona, 2019, September 8
LEARNING OBJECTIVES

1. Theoretical aspects of liver hypertrophy and Augmented Portal Vein Embolisation (aPVE)

2. To learn about technical aspect of aPVE

3. aPVE Techniques Vs Surgical Techniques
Portal vein embolization (PVE) still represent the mainstay of radiological techniques for liver hypertrophy and can increase the volume of the FLR by up to 45-50% within 3 to 8 weeks.


Shindoh, J., et al., Analysis of the efficacy of portal vein embolization for patients with extensive liver malignancy and very low future liver remnant volume, including a comparison with the associating liver partition with portal vein ligation for staged hepatectomy approach. JAm Coll Surg, 2013

Leung, U., et al., Remnant growth rate after portal vein embolization is a good early predictor of post-hepatectomy liver failure. JAm Coll Surg, 2014

Fadi R., Pim B. Olthof, MD, PhDa, Krijn P. van Lienden et Al. Functional and volumetric assessment of liver segments after portal vein embolization: Differences in hypertrophy response. Surgery 2019
Portal Vein Embolization leads to sufficient FLR hypertrophy in about 80% of patients, allowing them to undergo surgery from which they were initially rejected.

The two main reasons of non-resection after PVE are:
- tumor progression (≈ 15% of cases)
- FLR insufficient hypertrophy (≈ 5% of cases)
- aPVE

Piron L, Emmanuel Deshayes, Laure Escal, Regis Souche, Astrid Herrero Marie-Ange, Pierre don Foulonogne, Eric Assenat, Ngole Lam, François Quenet, Boris Guiu
Cancer. 2017
Porto-portal collaterals negatively influence hypertrophy after PVE
PORTAL FLOW VARIATIONS AFTER PVE

Portal Canals PVE Lobe

Portal Canals FLR Lobe
Collateral Left to Right Lobe Portal Perfusion

Porto-portal collaterals flow allow blood exchange also after PVE, PISA and right artery resection

*Surgical left gastric vein cannulation - Injection of 5ml indocyanine green (ICG)*
Minor injuries (<10% parenchymal involvement) induce only localized mitotic reactions while major injuries (>50% parenchymal involvement) result in multiple mitotic waves throughout the entire liver.


APVE

INCREASED BLOOD OVERFLOW TO THE FLR
REDUCED PERFUSION OF THE TUMOR BEARING LOBE
ASSOCIATING LIVER PARTITION AND PORTAL VEIN LIGATION FOR STAGED HEPATECTOMY
A literature review of associating liver partition and portal vein ligation for staged hepatectomy (ALPPS): so far, so good

Martin de Santibañes, Luis Boccalatte, Eduardo de Santibañes

Table 1: Patient's general characteristics, operative data, and outcomes in reports with 38 patients

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Country</th>
<th>N</th>
<th>Increase FLR (%)</th>
<th>Hospital stay (days)</th>
<th>Mortality (%)</th>
<th>Major morbidity (%)</th>
<th>Minor morbidity (%)</th>
<th>Follow-up months</th>
<th>Mortality (%)</th>
<th>Major morbidity (%)</th>
<th>Minor morbidity (%)</th>
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<tbody>
<tr>
<td>Schmittbaur et al.</td>
<td>2012</td>
<td>Switzerland</td>
<td>25</td>
<td>74</td>
<td>NR</td>
<td>6/8</td>
<td>44±</td>
<td>12±</td>
<td>6 (2-25)</td>
<td>90±</td>
<td>NR</td>
<td>NR</td>
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<tr>
<td>Marahdeh et al.</td>
<td>2012</td>
<td>Jordan</td>
<td>8</td>
<td>89</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
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<tr>
<td>Dorni et al.</td>
<td>2012</td>
<td>Switzerland</td>
<td>8</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
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<tr>
<td>Dobnik et al.</td>
<td>2012</td>
<td>Italy</td>
<td>8</td>
<td>76</td>
<td>42 (25-56)</td>
<td>93</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
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<tr>
<td>Torres et al.</td>
<td>2013</td>
<td>Italy</td>
<td>39</td>
<td>83</td>
<td>17.8 (15-40)</td>
<td>N/R</td>
<td>59</td>
<td>12±</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
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<tr>
<td>Li et al. [14]</td>
<td>2013</td>
<td>China</td>
<td>9</td>
<td>87.2</td>
<td>NR</td>
<td>1/9</td>
<td>22±</td>
<td>22±</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
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<tr>
<td>Restani et al.</td>
<td>2014</td>
<td>Italy</td>
<td>11</td>
<td>61</td>
<td>36 (27-73)</td>
<td>N/R</td>
<td>N/R</td>
<td>9±</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
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<tr>
<td>Nadali et al.</td>
<td>2015</td>
<td>Greece</td>
<td>15</td>
<td>87.2</td>
<td>NR</td>
<td>36±</td>
<td>40±</td>
<td>12±</td>
<td>NR</td>
<td>NR</td>
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<tr>
<td>Schmidt et al.</td>
<td>2015</td>
<td>Italy</td>
<td>6</td>
<td>64</td>
<td>29.2 (23-129)</td>
<td>83±±</td>
<td>40±</td>
<td>12±</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
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<tr>
<td>Hernández et al.</td>
<td>2015</td>
<td>Spain</td>
<td>14</td>
<td>93</td>
<td>38 (28–129)</td>
<td>36±</td>
<td>14±</td>
<td>0±</td>
<td>9.4</td>
<td>NR</td>
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<tr>
<td>Rizi et al.</td>
<td>2015</td>
<td>Italy</td>
<td>12</td>
<td>47</td>
<td>24 (16–62)</td>
<td>NR</td>
<td>41±</td>
<td>3±</td>
<td>12 (6–18)</td>
<td>67±</td>
<td>92±</td>
<td>NR</td>
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<tr>
<td>Lang et al.</td>
<td>2015</td>
<td>Italy</td>
<td>16</td>
<td>53.5</td>
<td>59 (36–94)</td>
<td>81±</td>
<td>3±</td>
<td>12±</td>
<td>26 (4–143)</td>
<td>NR</td>
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<td>NR</td>
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<tr>
<td>Ghoneim et al.</td>
<td>2015</td>
<td>Egypt</td>
<td>15</td>
<td>84.3</td>
<td>NR</td>
<td>6±</td>
<td>6±</td>
<td>6±</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
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<tr>
<td>Alvarez et al.</td>
<td>2015</td>
<td>Spain</td>
<td>30</td>
<td>89.7</td>
<td>16 (31–62)</td>
<td>53</td>
<td>45±</td>
<td>6.6</td>
<td>17 (1.5–35)</td>
<td>40±</td>
<td>63±</td>
<td>NR</td>
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<tr>
<td>Sommar et al.</td>
<td>2015</td>
<td>Italy</td>
<td>30</td>
<td>82</td>
<td>27 (13–152)</td>
<td>N/R</td>
<td>2±</td>
<td>26±</td>
<td>12±</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Björnsson et al.</td>
<td>2015</td>
<td>Iceland</td>
<td>33</td>
<td>65.3</td>
<td>49 (13–195)</td>
<td>6±±±</td>
<td>45±±±</td>
<td>4.5±±±</td>
<td>22.5</td>
<td>22±</td>
<td>92±</td>
<td>NR</td>
</tr>
<tr>
<td>Vezzoni et al.</td>
<td>2015</td>
<td>Italy</td>
<td>9</td>
<td>96</td>
<td>22 (13–36)</td>
<td>67±</td>
<td>44±</td>
<td>11±</td>
<td>17± (8.6–25.6)</td>
<td>75±</td>
<td>99±</td>
<td>NR</td>
</tr>
</tbody>
</table>

Updates Surg, 2016 Oct 20
Since evidence have been cumulating that additional morbidity associated to ALPPS could depend on the surgical burden of stage-1 some modifications have been proposed:

✓ **Partial-ALPPS (p-ALPPS)**

✓ **Lasparoscopic approach of the portal vein ligation**

✓ **Associating Liver Tourniquet and right Portal occlusion for Staged hepatectomy technique (ALTPS)**

✓ **Laparoscopic microwave Ablation and Portal vein ligation for Staged hepatectomy (LAPS)**

✓ «Hybrid ALPPS» (Surgical split and delayed PVE)

✓ ......
Schadde et al. demonstrated that liver failure developed in 31% of patients with sFLR of 30% to 40% and in 16% of patients with sFLR > 40% prior to stage 2 in the ALPPS registry.

Histologic features after surgery associating liver partition and portal vein ligation for staged hepatectomy versus those after hepatectomy with portal vein embolization

Kenichi Matsuo, MD, PhD, Takashi Murakami, MD, Daisuke Kawaguchi, MD, Yukihiro Hiroshima, MD, PhD, Keiji Koda, MD, PhD, Kazuto Yamazaki, MD, PhD, Yasuo Ishida, MD, PhD, and Kuniya Tanaka, MD, PhD, Chiba, Japan

“In the FLR, regenerative hepatocytes in ALPPS were morphologically immature compared with PVE.”

ALPPS should be performed with caution, considering limited functional increase in the FLR reflecting immaturity of the regenerative hepatocytes.
Augmented Portal Vein Embolisation

Stage-1 ALPPS

PVE + EVLD

PVE + PISA
Percutaneous PVE was achieved via an ipsilateral approach through the tumour-bearing liver by accessing the segment V portal vein branch under US guidance and local anaesthesia.

- Mixture of cyanoacrylate and iodized oil (ratio 1/5 - 1/6)
- **Deep Sedation**
- Multiple ablation cycles for each insertion line
- **Fan Shaped Ablation Area**
- Multiple or single access sites were used to allow sequential overlapping of ablative fields
Giant mts from parotid adenoid cystic carcinoma in a obese female patient 53 y.o.
PISA Technique: Landmarks

- MHV
- IVC
- Right Lobe Lesion
PISA Technique: Landmarks (II)

- Right Lobe Lesion
- Gallbladder
- Microwave Antenna Tip
SAFETY: ABLATION AREA - MIDDLE HEPATIC VEIN

MHV

Microwave Antenna Tip

IVC

4 Insertion Point
SAFETY: ABLATION AREA - MIDDLE HEPATIC VEIN (IV)
CEUS: ABLATED AREA

The First One Pt

Contrast-Enhanced Ultrasound
Correspondence between the ultrasound image without and with contrast medium
T0 FLR Volume 460cm³
FLR/BW 0,48
FLR/tFLV 24%

21d AFTER PVE
FLR 30%
FLR/BW 0,63
FLR/tFLV 35%

2Week after PISA
FLR 78%
FLR/BW 0,82
FLR/tFLV 52%
99mTc-Mebrofenin Hepatobiliary Scintigraphy (HBS)
99mTc – HIDA: LIVER FUNCTION
INSIDE THE OPERATING ROOM: ABLATIVE NECROSIS
Surgical Resection on Ablative Plane

➢ Ablative necrosis after 2 weeks allow easy tissue dissection and easy detection of biliary vessels for prevention of postoperative leakage or biloma.

➢ No Pringle maneuver needed during resection plane creation and substantial reduction in bleeding.
9 Ablation Lines
The PISA procedure allow to reach a FLR volume to body weight ratio >0.8 in all patients
Fig. 6 Graph reports the FLR volume increase in time. The procedures are highlighted by the vertical yellow arrows, whereas the white arrows indicate the CT assessment 21 days after PVE and 10 days after the PISA procedure.
FLR KINETIC GROWTH RATE

- PVE: 5.5-7 cm³/day
- PISA: 14.19 cm³/day
- EVLD: Before PVE
- CT: Before PISA
- T0: Before PVE
- T1: CT 1st day
- T2: PISA
- T3: EVLD
- T4: Preoperative CT
- T5: FLR Volume after resection

Confirmed
RESULTS

EFFICACY: FLR HYPERTROPHY

- Average percentages of FLR volume hypertrophy associating PVE and PISA: 83% (68.1% to 109.3%)
- KINETIC GROWTH RATE after PVE
  - 6.1 cm³/day [range 5.4-6.7 cm³/day]
- KINETIC GROWTH RATE after PISA
  - 17.0 cm³/day [range 14.0-19.0 cm³/day]  

A.Lunardi, U Boggi et al.  
Feasibility of Percutaneous Intrahepatic Split by Microwave Ablation (PISA) After Portal Vein Embolization for Hypertrophy of Future Liver Remnant: The Radiological Stage-1 ALPPS  
CVIR 2018
➢ **PVE:** up to 40-45% within 3 to 8 weeks


➢ **PVE + eLVD:** 53% at 1 week  63% at 3 weeks


➢ **PVE + PISA:** 83% (68.1% to 112%) 3 weeks


➢ **Stage 1 ALPPS:** 75 % (47% to 96%) 1-2 weeks

*Martin de Santibañes, Luis Boccalatte, Eduardo de Santibañes. A literature review of associating liver partition and portal vein ligation for staged hepatectomy (ALPPS): so far, so good. Updates Surg, 2016*
<table>
<thead>
<tr>
<th>Combination</th>
<th>FLR Kinetic Growth Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALPPS</td>
<td>25.4-32.7 cc/day (4)</td>
</tr>
<tr>
<td>PVE + eLVD</td>
<td>25 ± 8 cc/day (2)</td>
</tr>
<tr>
<td>PVE+ PISA</td>
<td>17 ± 3 cc/day (1)</td>
</tr>
<tr>
<td>PVE + LVD</td>
<td>9.3 cc/day (2)</td>
</tr>
<tr>
<td>PVE alone</td>
<td>4.4 cc/day (2-3)</td>
</tr>
<tr>
<td>PV Ligation</td>
<td>3 cc/day (3)</td>
</tr>
</tbody>
</table>


Bilirubin level did not increase after procedures
- Minimal variation of PT-INR after PVE and after PISA
- Fast liver function recovery after surgery
Therapeutic algorithm of patients affected by liver malignancies and candidate to major liver resection, with an insufficient functional reserve of the FLR.

FIRST 3 Pts
RESCUE PISA:
INDADEQUATE VOLUME
21d AFTER PVE

Selection of eligible patients

PVE

3 weeks after PVE: CT scan

FLR volume sufficient?

yes

Surgery

no

PISA

HBS*

Surgery

7-10 days after PISA: CT scan

* HEPATO-BILIARI SCINTIGRAPHY
Selection of eligible patients

PVE

day 6 - CT scan

Primary PISA
FLR/TFLV < 25%
FLR/BW < 0.5

Intraoperative FLR Biopsy

HBS*

Surgery

US-Guided Core Needle Biopsy

day 7 PISA

day 20 - CT scan

Therapeutic algorithm of patients candidated to major liver resection, with an insufficient functional reserve of the FLR.
Microwave System 1

3 pt
60W ablation cycle (60-180s)
The mean total ablation time was
26.8 min (range 16–37.5 min)

Progressive anemia after ablation
Hb Decrease from 1.5mg/dl to 3 mg/dl (915Mhz)

Microwave System 2

6 pt
80W ablation cycle (50-100s)
The mean total ablation time was
12 min (range 7–18 min)

No anemia
(2450 MHz)
9 Patients Treated (no procedure related complication)
1 Refused resection (Geova Witness)
1 Patients are waiting for resection during this Month
7 Patients have been Successfully Resected
After Resection 1 Patient had Post Hepatectomy Liver Failure (PHLF)
Value of aPVE

✓ Feasible and safe
✓ Low morbidity - Short Hospital stay
✓ No mortality aPVE related
✓ aPVE does not completely exclude other alternative medical treatments…
✓ …reduced liver functional reserve for chemotherapy

NEED FOR UPDATED STUDY
✓ Criteria for Patients Selection
✓ Liver Volume, Liver Function, Tissue Quality (histology)
✓ Slow Vs Fast Kinetic Rate Hypertrophy?
✓ Outcome Prediction - Clinical/Oncological Scenario!
PERCUTANEOUS INTRAHEPATIC SPLIT BY MICROWAVE ABLATION (PISA)

ALESSANDRO LUNARDI, MD