ILCA Symposium 2: Perihilar cholangiocarcinoma

- Patient selection and optimization for surgery -

Masato Nagino, MD
Department of Surgery
Nagoya University Graduate School of Medicine
- GEM vs. GEM+CDDP for relapsed / unresectable biliary cancer -

<table>
<thead>
<tr>
<th>Months since randomization</th>
<th>Overall survival (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>GEM</td>
</tr>
<tr>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>20</td>
<td>206</td>
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<tr>
<td>40</td>
<td>151</td>
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<tr>
<td>60</td>
<td>97</td>
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<tr>
<td>80</td>
<td>53</td>
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<tr>
<td>100</td>
<td>28</td>
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<tr>
<td>120</td>
<td>15</td>
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<tr>
<td>140</td>
<td>4</td>
</tr>
<tr>
<td>160</td>
<td>3</td>
</tr>
<tr>
<td>180</td>
<td>2</td>
</tr>
</tbody>
</table>

MST: GEM 8.1m, GEM + CDDP 11.7m

Hazard ratio for death: 0.64 (95% CI 0.52-0.80)  
P<0.001
- GEM vs. GEM+CDDP for relapsed / unresectable biliary cancer -

- Overall survival (%)
  - GEM
  - GEM + CDDP

- Hazard ratio for death
  - MST 8.1m
  - MST 11.7m
  - Effective ?

- No. at Risk
  - GEM: 206, 151, 97, 53, 28, 15, 4, 3, 2
  - GEM + CDDP: 204, 167, 120, 76, 51, 28, 17, 8, 2

- Hazard ratio for death (95% CI)
  - 0.64 (0.52-0.80)
  - P<0.001
Chemotherapy is much less effective; No patients cured.
Review of our experience

Mt. Fuji
Number of resection of perihilar cholangiocarcinoma
Number of resection of perihilar cholangiocarcinoma

- 100
- 200
- 300
- 400
- 500
- 600
- 700
- 800
- 900
- 1000

- 1980
- 1990
- 1995
- 2000
- 2005
- 2010
- 2015
- 2020
- 2019

- 622

- 400
Perihilar cholangiocarcinoma
- January 1977 ~ December 2015, Nagoya University -

Total number of perihilar cholangiocarcinoma treated [n=1077]

Laparotomy [n=912]

Inoperable [n=165]

Unresectable [n=81]

Not resected [n=246, 23%]

Resected [n=831, 77%]

- pM0 and R0 [n=575]
- pM0 and R1/2 [n=134]
- pM1 (=stage IVB) [n=122]
831 consecutive resections include

Bismuth type I / II = 133 (16.0%)
Bismuth type III = 307 (36.9%)
Bismuth type IV = 391 (47.1%)
Trend of surgical procedure

More extended surgery

1. **Left trisectionectomy**

2. **Portal vein resection**

3. **Anatomic right trisectionectomy**

4. **Hepatic artery resection**

5. **Hepatopancreatoduodenectomy**
Surgical treatment of perihilar cholangiocarcinoma

Type of hepatectomy (1977~2015, n=831)

Surgical treatment of perihilar cholangiocarcinoma

Combined resection (1977~2015, n=831)

- 2000 (n=188)
- 2001~05 (n=168)
- 2006~10 (n=218)
- 2011~15 (n=257)

<table>
<thead>
<tr>
<th>PD</th>
<th>PV resection</th>
<th>HA resection</th>
</tr>
</thead>
<tbody>
<tr>
<td>22 (12%)</td>
<td>57 (30%)</td>
<td>5 (3%)</td>
</tr>
<tr>
<td>20 (12%)</td>
<td>58 (35%)</td>
<td>25 (15%)</td>
</tr>
<tr>
<td>32 (15%)</td>
<td>89 (41%)</td>
<td>46 (21%)</td>
</tr>
<tr>
<td>30 (12%)</td>
<td>87 (34%)</td>
<td>56 (22%)</td>
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</tbody>
</table>
Surgical treatment of perihilar cholangiocarcinoma

<table>
<thead>
<tr>
<th>Period</th>
<th>Time (minutes)</th>
<th>Blood loss (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1979～1985 (n=25)</td>
<td>648±181</td>
<td>4450±3543</td>
</tr>
<tr>
<td>1986～1990 (n=41)</td>
<td>673±151</td>
<td>4394±2329</td>
</tr>
<tr>
<td>1991～1995 (n=42)</td>
<td>858±249</td>
<td>5367±3450</td>
</tr>
<tr>
<td>1996～2000 (n=66)</td>
<td>760±159</td>
<td>2782±2234</td>
</tr>
<tr>
<td>2001～2005 (n=165)</td>
<td>674±145</td>
<td>1902±1270</td>
</tr>
<tr>
<td>2006～2010 (n=216)</td>
<td>605±134</td>
<td>1768±1130</td>
</tr>
<tr>
<td>2011～2015 (n=243)</td>
<td>598±128</td>
<td>1273±893</td>
</tr>
</tbody>
</table>
## Surgical treatment of perihilar cholangiocarcinoma

### Mortality (including all deaths related to surgery)

<table>
<thead>
<tr>
<th>Period</th>
<th>No. of resection</th>
<th>90-day mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>1977～1985</td>
<td>29</td>
<td>4 (13.8%)</td>
</tr>
<tr>
<td>1986～1990</td>
<td>43</td>
<td>4 (9.3%)</td>
</tr>
<tr>
<td>1991～1995</td>
<td>49</td>
<td>4 (8.2%)</td>
</tr>
<tr>
<td>1996～2000</td>
<td>67</td>
<td>7 (10.4%)</td>
</tr>
<tr>
<td>2001～2005</td>
<td>168</td>
<td>5 (3.0%)</td>
</tr>
<tr>
<td>2006～2010</td>
<td>218</td>
<td>3 (1.4%)</td>
</tr>
<tr>
<td>2011～2015</td>
<td>257</td>
<td>5 (1.9%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>831</strong></td>
<td><strong>32 (3.9%)</strong></td>
</tr>
</tbody>
</table>
Surgical treatment of perihilar cholangiocarcinoma

All resections (n = 831)

No at risk

Years after surgery

831 317 176 59

50% 36% 25% 25%
Surgical treatment of perihilar cholangiocarcinoma

All resections, according to time period (n = 831)

- A: 2008 ~ 2015
- B: 2001 ~ 2007
- C: 1977 ~ 2000

No at risk:
- A: 390
- B: 253
- C: 188

Years after surgery:
- 0: 47
- 1: 36
- 2: 23
- 3: 14
- 4: 25
- 5: 34
- 6: 36
- 7: 47
- 8: 61
- 9: 46
- 10: 34%
Surgical treatment of perihilar cholangiocarcinoma

R0 / pN0 / pM0 patients, according to time period (n = 356)

- **A:** 2008 ~ 2015
- **B:** 2001 ~ 2007
- **C:** 1977 ~ 2000

Years after surgery:

- **A:** 172
- **B:** 105
- **C:** 79

No at risk:

- **A:** 85
- **B:** 75
- **C:** 45

* *, Logrank test

P values:

- **P = 0.224***
- **P < 0.001***
Surgical treatment of perihilar cholangiocarcinoma

R0 / pN1 / pM0 patients, according to time period (n = 219)

No at risk

<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td>0</td>
<td>109</td>
<td>69</td>
<td>41</td>
</tr>
<tr>
<td>1</td>
<td>28</td>
<td>22</td>
<td>15</td>
</tr>
<tr>
<td>2</td>
<td>9</td>
<td>13</td>
<td>6</td>
</tr>
<tr>
<td>3</td>
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<tr>
<td>4</td>
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<td>9</td>
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<td></td>
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<tr>
<td>10</td>
<td></td>
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</tr>
</tbody>
</table>

Years after surgery

A: 2008~2015
B: 2001~2007
C: 1977~2000

P = 0.904*
P = 0.026*

*, Logrank test
Surgical treatment of perihilar cholangiocarcinoma

R0 / pN1 / pM0 patients, according to time period (n = 219)

No at risk
A: 109
B: 69
C: 41

Years after surgery
0 1 2 3 4 5 6 7 8 9 10
0 10 20 30 40 50 60 70 80 90 100

A: 2008 ~ 2015
B: 2001 ~ 2007
C: 1977 ~ 2000

P = 0.904*
P = 0.026*

*, Logrank test

P = 0.904*
P = 0.026*
Surgical treatment of perihilar cholangiocarcinoma

R0 / pN1 / pM0 patients, according to time period (n = 219)

A: 2008 ~ 2015
B: 2001 ~ 2007
C: 1977 ~ 2000

P = 0.904*
P = 0.026*

*, Logrank test

Gem + CDDP in ABC-02 trial

No at risk
A: 109
B: 69
C: 41

Years after surgery

No at risk
A: 28
B: 22
C: 15

Years after surgery

No at risk
A: 9
B: 13
C: 6

Years after surgery

No at risk
A: 5
B: 4
C: 4
Surgical treatment of perihilar cholangiocarcinoma

R1・2 / pM0, according to time period (n = 134)

A: 2008～2015
B: 2001～2007
C: 1977～2000

No at risk
A: 68  15  3
B: 37  12  6
C: 29  5  1

Years after surgery

* Logrank test

P = 0.067*
P < 0.001*
P = 0.484*
Surgical treatment of perihilar cholangiocarcinoma

R1・2 / pM0, according to time period (n = 134)

*Logrank test

A: 2008～2015
B: 2001～2007
C: 1977～2000

Gem + CDDP in ABC-02 trial

No at risk
A: 68  15  3
B: 37  12  6
C: 29  5  1

Years after surgery

(%)

Years after surgery

No at risk

A: 68
B: 37
C: 29

P = 0.067*
P = 0.484*
P < 0.001*
Surgical treatment of perihilar cholangiocarcinoma

**pM1**, according to time period (n = 122)

No at risk

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>No</td>
<td>41</td>
<td>42</td>
<td>39</td>
</tr>
<tr>
<td>9</td>
<td>31</td>
<td>33</td>
<td>33</td>
</tr>
<tr>
<td>2</td>
<td>28</td>
<td>29</td>
<td>28</td>
</tr>
<tr>
<td>3</td>
<td>25</td>
<td>26</td>
<td>25</td>
</tr>
</tbody>
</table>

P = 0.004* for A vs. B and P = 0.886* for A vs. C

*, Logrank test
Surgical treatment of perihilar cholangiocarcinoma

Gem + CDDP in ABC-02 trial

8% 34%

Years after surgery

No at risk

A: 41 9
B: 42 3 2
C: 39 3 3

pM1, according to time period (n = 122)

A: 2008 ~ 2015
B: 2001 ~ 2007
C: 1977 ~ 2000

P = 0.004*
P = 0.886*

*, Logrank test
Surgical treatment of perihilar cholangiocarcinoma

**pM1**, according to time period (n = 122)

- **A**: 2008 ~ 2015
  - No at risk: 41, 9
  - P = 0.886*

- **B**: 2001 ~ 2007
  - No at risk: 42, 3
  - P = 0.004*

- **C**: 1977 ~ 2000
  - No at risk: 39, 3

*Logrank test

Gem + CDDP in ABC-02 trial

Years after surgery

No at risk
- A: 41
- B: 42
- C: 39

Years after surgery: 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10

Percentage: 0%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%
Surgical treatment of perihilar cholangiocarcinoma

Liver metastasis or dissemination (n = 122) according to site of distant metastasis.

Gem + CDDP in ABC-02 trial.

Years after surgery:
- No at risk
  - A: 53
  - 48%
  - 23
  - 6%
  - 2
Surgical treatment of perihilar cholangiocarcinoma

**pm1**, according to the site of distant metastasis (n = 122)

No at risk

<table>
<thead>
<tr>
<th>A: Liver metastasis or dissemination</th>
<th>No at risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>53</td>
<td>23</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>B: Distant node metastasis alone</th>
<th>No at risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>69</td>
<td>41</td>
</tr>
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*Logrank test, P = 0.002*

Gem + CDDP in ABC-02 trial
Summary of our data 1

1. Extended resection based strategy
   - 96% of patients underwent major Hx. with caudate lobectomy.
   - 40% of patients underwent combined PV resection.
   - 21% of patients underwent combined HA resection.
   - 13% of patients underwent combined pancreatoduodenectomy.

2. Blood loss and mortality decreased year by year
   - For the most recent 10 years,
   - Blood loss was 1506 mL on the average, and
   - 90-day mortality was 1.7% (=8/475).
Summary of our data 2

3. Survival after resection was improved year by year

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>All patients</td>
<td>23%</td>
<td>36%</td>
<td>47%</td>
</tr>
<tr>
<td>N0R0M0</td>
<td>43%</td>
<td>66%</td>
<td>70%</td>
</tr>
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<td>15%</td>
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Summary of our data 2

3. Survival after resection was improved year by year

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<th>5-year survival</th>
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<td>All patients</td>
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### Surgical treatment of perihilar cholangiocarcinoma

**Summary of our data 2**

#### 3. Survival after resection was improved year by year

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Resection should be indicated even in patients with node metastasis.
Surgical treatment of perihilar cholangiocarcinoma

Summary of our data 2

3. Survival after resection was improved year by year

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Resection is somewhat beneficial even in R1/2 resection
4. Distant node metastasis may be a candidate of resection

Survival of pts. with liver metastasis and/or dissemination was dismal even after Resection. However, survival of pts. with distant node metastasis alone was unexpectedly better with 11% at 5 years.
4. Distant node metastasis may be a candidate of resection

Survival of pts. with liver metastasis and/or dissemination was dismal even after resection. However, survival of pts. with distant node metastasis alone was unexpectedly better with 11% at 5 years.

When distant node is preoperative PET positive ➔ inoperable.

When distant node is preoperative PET negative but frozen positive ➔ resection
Chemotherapy is much less effective; No patients cured.

Strategy is to “pursue resectability with never give up spirit”
Patient selection from a viewpoint of liver function
How to evaluate functional reserve

Liver volume

FLR (%)

Liver function

ICGK
How to evaluate functional reserve

Liver volume $\times$ Liver function

FLR (%) $\times$ ICGK

“ICGK-F”

How to evaluate functional reserve

Liver volume \times \text{Liver function}

FLR (%) \quad \text{ICGK}

"ICGK-F"

0.05 or more is safe criteria of Hx.

How to evaluate functional reserve

PVE \downarrow \text{Liver volume} \times \text{Liver function} \downarrow \text{Biliary drainage}

\text{FLR (\%)} \quad \text{ICGK}

“ICGK-F”

0.05 or more is safe criteria of Hx.

Patients with perihilar cholangiocarcinoma
(666 patients between 2006 and 2015)

Candidates of right trisectionectomy
N=65

- No-PVE due to FLR>40%, n=6
  (These 6 pts underwent resection)

With PVE
N=59

- Progressive disease, n=3

Assessment of FLR
N=56

- Poor liver function, n=5

Laparotomy
N=51

- Unresectable, n=9

Right trisectionectomy
N=42

Combined resections
PV n=25
HA n=1
PD n=3
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(666 patients between 2006 and 2015)

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  - With PVE
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      - Progressive disease, n=3
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          - Poor liver function, n=5
          - Laparotomy
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  - With PVE
    - N=59
      - Combined resections
        - PV n=25
        - HA n=1
        - PD n=3
Baseline characteristics of 56 study patients who received PVE prior to surgery

<p>| | | |</p>
<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>67</td>
<td>(48-80)</td>
</tr>
<tr>
<td>Gender</td>
<td>men 35; women 21</td>
<td></td>
</tr>
<tr>
<td>Bismuth type</td>
<td>IV 47; III 7; II 2</td>
<td></td>
</tr>
<tr>
<td>ICGK</td>
<td>0.164</td>
<td>(0.100 – 0.225)</td>
</tr>
<tr>
<td>FLR (mL)</td>
<td>287</td>
<td>(141 – 642)</td>
</tr>
<tr>
<td>FLR (%)</td>
<td>25</td>
<td>(14 – 41)</td>
</tr>
<tr>
<td>ICGK-F</td>
<td>0.037</td>
<td>(0.021 – 0.068)</td>
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</table>

**Distribution of %FLR**

**Distribution of ICGK-F**
Pre-PVE characteristics of 56 study patients who received PVE prior to surgery

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value (Range)</th>
</tr>
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<tbody>
<tr>
<td>Age (years)</td>
<td>67 (48-80)</td>
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<td>ICGK*</td>
<td>0.164 (0.100 – 0.225)</td>
</tr>
<tr>
<td>FLR (mL)</td>
<td>287 (141 – 642)</td>
</tr>
<tr>
<td>FLR (%)</td>
<td>25 (14 – 41)</td>
</tr>
<tr>
<td>ICGK-F*</td>
<td>0.037 (0.021 – 0.068)</td>
</tr>
</tbody>
</table>

**Distribution of %FLR**

- FLR ≤ 25% n=29 (52%)

**Distribution of ICGK-F**

- ICGK-F ≤ 0.04 n=27 (48%)
## Details of PVE performed \( (n=56) \)

<table>
<thead>
<tr>
<th>Type of PVE</th>
<th>Right + P4 ( (n=41, 73%) ); Right alone ( (n=15, 27%) )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Embolic materials</td>
<td>Ethanol ( (n=40) ) or gelatin sponge ( (n=16) ) + steel coils</td>
</tr>
<tr>
<td>Operating time</td>
<td>2.1 hours ( (0.9 \text{ – } 4.0 \text{ hours}) )</td>
</tr>
<tr>
<td>Complications*</td>
<td>7 ( (13%) )</td>
</tr>
<tr>
<td>Re-canalization</td>
<td>9 ( (16%) )</td>
</tr>
<tr>
<td>Re-PVE</td>
<td>5 ( (9%) )</td>
</tr>
<tr>
<td>Mortality</td>
<td>0</td>
</tr>
</tbody>
</table>

* biloma \( (n=2) \), hepatic artery injury \( (n=2) \), intraabdominal bleeding \( (n=1) \), PV thrombus \( (n=1) \), and peeled guidewire \( (n=1) \), with overlaps.
Changes in volume after PVE:
Right trisegment (R3) PVE vs. Right (R2) PVE

Volume of left medial segment

Volume of left lateral segment

Changes in volume after PVE:
Right trisegment (R3) PVE vs. Right (R2) PVE

Volume of left medial segment

Volume of left lateral segment

122 ± 39 cm³ volume gain
66 ± 35 cm³ volume gain

## Effect of PVE (n=56)

<table>
<thead>
<tr>
<th></th>
<th>Before PVE</th>
<th>After PVE</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total liver volume (mL)</td>
<td>1146 (707-2265)</td>
<td>1161 (797-2023)</td>
<td>NS</td>
</tr>
<tr>
<td>FLR (mL)</td>
<td>287 (141-642)</td>
<td>380 (223-702)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FLR (%)</td>
<td>24.8 (13.8-41.4)</td>
<td>33.8 (19.1-46.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ICGK</td>
<td>0.163 (0.100-0.225)</td>
<td>0.162 (0.088-0.217)</td>
<td>NS</td>
</tr>
<tr>
<td>ICGK-F</td>
<td>0.037 (0.021-0.068)</td>
<td>0.056 (0.027-0.083)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>$\triangle$ICGK-F</td>
<td>-</td>
<td>0.014 (-0.07-0.39)</td>
<td></td>
</tr>
</tbody>
</table>
Final assessment of ICGK-F

<table>
<thead>
<tr>
<th></th>
<th>Resected (n=42)</th>
<th>Unresected (n=9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No laparotomy</td>
<td>16% (n=9)</td>
<td></td>
</tr>
<tr>
<td>Laparotomy</td>
<td>20% (n=11)</td>
<td></td>
</tr>
</tbody>
</table>

No laparotomy due to poor functional reserve (n=5)

Laparotomy (n=51)
Final assessment of ICGK-F

- No laparotomy due to poor functional reserve (n=5)
  - Resected (n=42) 16% (n=9)
  - Unresected (n=9) 20% (n=11)

- Laparotomy (n=51)
Final assessment of ICGK-F

- No laparotomy due to poor functional reserve (n=5)
  - Resected (n=42): 16%
  - Unresected (n=9): 20%
- Laparotomy (n=51)
Final assessment of ICGK-F

No laparotomy due to poor functional reserve (n=5)

Laparotomy (n=51)

- Resected (n=42)
- Unresected (n=9)

20% (n=11)

16% (n=9)
Final assessment of ICGK-F

- Final ICGK-F

- Resected (n=42)
- Unresected (n=9)

- No laparotomy due to poor functional reserve (n=5)

- Laparotomy (n=51)

- 20% (n=11) for Laparotomy

- 16% (n=9) for No laparotomy due to poor functional reserve
**Postoperative liver-associated morbidity**
in 42 patients who underwent right hepatic trisectionectomy

<table>
<thead>
<tr>
<th>ISGLS PHLF</th>
<th>Grade B</th>
<th>Grade C</th>
<th>Refractory ascites</th>
<th>Postoperative FFP</th>
<th>In-hospital mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>10</td>
<td>4</td>
<td>7</td>
<td>9</td>
<td>1*</td>
</tr>
<tr>
<td></td>
<td>(24%)</td>
<td>(10%)</td>
<td>(15%)</td>
<td>(21%)</td>
<td>(2%)</td>
</tr>
</tbody>
</table>

ISGLS, international Study Group of Liver Surgery;
POLF, postoperative liver failure

*, a 78-year-old man died of liver failure 44 days after surgery (FLR 34%, ICGK-F 0.067)
### Surgical outcome of pts. with ICGK-F ≤ 0.04

<table>
<thead>
<tr>
<th></th>
<th>78, M</th>
<th>63, M</th>
<th>64, M</th>
</tr>
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<tbody>
<tr>
<td><strong>Initial assessment</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FLR (mL)</td>
<td>141</td>
<td>194</td>
<td>422</td>
</tr>
<tr>
<td>FLR (%)</td>
<td>13.8</td>
<td>18.0</td>
<td>23.4</td>
</tr>
<tr>
<td>ICGK</td>
<td>0.184</td>
<td>0.164</td>
<td>0.128</td>
</tr>
<tr>
<td>ICGK-F</td>
<td>0.025</td>
<td>0.030</td>
<td>0.030</td>
</tr>
<tr>
<td><strong>Final assessment</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(days after PVE)</td>
<td>(47)</td>
<td>(20)</td>
<td>(29)</td>
</tr>
<tr>
<td>FLR (mL)</td>
<td>296</td>
<td>250</td>
<td>572</td>
</tr>
<tr>
<td>FLR (%)</td>
<td>25</td>
<td>25</td>
<td>30</td>
</tr>
<tr>
<td>ICGK-F</td>
<td>0.031</td>
<td>0.039</td>
<td>0.400</td>
</tr>
<tr>
<td>PV resection</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Blood loss (L)</td>
<td>1.3</td>
<td>1.7</td>
<td>1.3</td>
</tr>
<tr>
<td>Operating time (hr)</td>
<td>11.0</td>
<td>8.4</td>
<td>11.4</td>
</tr>
<tr>
<td>Maximal TB (mg/dL)</td>
<td>16.0</td>
<td>4.5</td>
<td>5.7</td>
</tr>
<tr>
<td>Total FFP (U)</td>
<td>15</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Ascites</td>
<td>+++</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Hospital stay (days)</td>
<td>64</td>
<td>22</td>
<td>64</td>
</tr>
<tr>
<td>Follow-up</td>
<td>5.0m, dead</td>
<td>8.1y, alive</td>
<td>1.5y, alive</td>
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<tr>
<td>Liver failure</td>
<td>NED</td>
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<td>AWD</td>
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NED, no evidence of disease; AWD, alive with disease
Surgical outcome of pts. with ICGK-F ≤ 0.04

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NED, no evidence of disease; AWD, alive with disease
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</tr>
</tbody>
</table>

|                  |         |         |         |
| PV resection     | +       | +       | -       |
| Blood loss (L)   | 1.3     | 1.7     | 1.3     |
| Operating time (hr) | 11.0   | 8.4     | 11.4    |
| Maximal TB (mg/dL)| 16.0   | 4.5     | 5.7     |
| Total FFP (U)    | 15      | 0       | 4       |
| Ascites          | +++     | ++      | +       |
| Hospital stay (days) | 64    | 22      | 64      |
| Follow-up        | 5.0m, dead | 8.1y, alive | 1.5y, alive |

Liver failure: NED, no evidence of disease; AWD, alive with disease
Summary
PVE prior to right hepatic trisectionectomy for perihilar CC

• Half of patients had a low ICGK-F ≤ 0.04 at initial presentation.
• PVE significantly increased functional capacity.
• 5 (9%) patients were not indicated for surgery because of the final ICGK-F of <0.04.
• Pts. with Initial ICGK of ≤0.03 may not be candidate of surgery.
• Pts. with final ICGK-F≥0.04 are good candidate of surgery.
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- Pts. with initial ICGK of ≤0.03 may not be candidate of surgery.
- Pts. with final ICGK-F ≥0.04 are good candidate of surgery.

PVE is essential to increase liver functional reserve and operative safety in patients undergoing extended hepatectomy.
PVE ?
ALPPS ?
ALPPS: Innovation for innovation’s sake

Jacques Belghiti, MD, a,b,c Safi Dokmak, MD, a,b,c and Erik Schadde, MD, d,e Paris, France, Chicago, IL and Canton of Zurich, Switzerland

From the Department of HPB Surgery and Liver Transplantation, a Beaujon Hospital, Assistance Publique, Hôpitaux de Paris, b and Université Paris VII Denis Diderot, c Paris, France; and Department of Surgery, Division of Transplantation, d Rush University Medical Center, Chicago, IL and Department of Surgery, e Cantonal Hospital Winterthur, Canton of Zurich, Switzerland

Hepatic resection and ablative procedures, which remain the mainstay treatment for patients with resectable colorectal liver metastases (CRLMs), can be facilitated by preoperative volumetric modulation when an insufficient liver remnant and/or diseased parenchyma are anticipated. The massive and rapid hypertrophy of the future liver remnant induced by the first stage of the in situ-split hepatectomy, is attributed to both portal diversion and parenchymal transection. The acceleration of purely volumetric growth allows the liver to be resected within few days during the same hospital stay, minimizing consequences also shows that the hepatocytes that regenerate early after the ALPPS procedure are smaller and less mature and may not function entirely normally. The greater mortality rate of ALPPS is associated with substantial postoperative complications and long hospital stays, which may well jeopardize the oncologic prognosis, in particular by delaying adjuvant treatments. Therefore, the gigantic lack of information on survival of patients operated by ALPPS should lead to the utmost caution before this approach is to be considered as an alternative to traditional strategies, which have been proven to be efficient in the long-term.
Concerns on the use of ALPPS for hilar CC

#1. Bile is colonized / infected, due to biliary drainage → infectious complication
#2. Bile contains cancer cell → peritoneal dissemination
#3. Hilar CC is a slow growing tumor → there is time to wait after PVE

Nagino M. Br J Surg (in press)
Concerns on the use of ALPPS for hilar CC

#1. Bile is colonized / infected, due to biliary drainage

→ infectious complication

#2. Bile contains cancer cell

We should use PVE !!

ALPPS is contraindicated !!

#3. Hilar CC is a slow-growing tumor

→ there is time to wait after PVE
Climbing ALPPS is not safe

Klatskin mountain (8888m), Switzerland
Patient selection from a viewpoint of age
Surgical treatment of perihilar cholangiocarcinoma

Age distribution in 831 resected patients

- 80 years ~
- 70 ~ 79 years
- 60 ~ 69 years
- 50 ~ 59 years
- ~49 years

- 1979-1990 (n=72)
  - 22%
  - 33%
  - 13%
  - 27%
  - 31%

- 1991-2000 (n=116)
  - 41%
  - 26%
  - 22%
  - 10%
  - 22%

- 2001-2005 (n=168)
  - 4%
  - 5%
  - 33%
  - 14%
  - 23%

- 2006-2010 (n=218)
  - 38%
  - 36%
  - 10%
  - 7%
  - 10%

- 2011-2015 (n=257)
  - 9%
  - 42%
  - 33%
  - 6%
  - ~49 years
Surgical treatment of perihilar cholangiocarcinoma

Age distribution in 831 resected patients

<table>
<thead>
<tr>
<th>Year Range</th>
<th>Percentage</th>
<th>Age Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>1979-1990</td>
<td>31%</td>
<td>60-69</td>
</tr>
<tr>
<td>1991-2000</td>
<td>33%</td>
<td>70-79</td>
</tr>
<tr>
<td>2001-2005</td>
<td>38%</td>
<td>80+</td>
</tr>
<tr>
<td>2006-2010</td>
<td>36%</td>
<td>60-69</td>
</tr>
<tr>
<td>2011-2015</td>
<td>33%</td>
<td>70-79</td>
</tr>
</tbody>
</table>

(n=72, n=116, n=168, n=218, n=257)
Age distribution in 831 resected patients

- 49 years: 5% (2001-2005, n=168)

Surgical treatment of perihilar cholangiocarcinoma
Surgical treatment of perihilar cholangiocarcinoma

Age distribution in 831 resected patients

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>50~59 years</td>
<td>22%</td>
<td>10%</td>
<td>10%</td>
<td>7%</td>
<td>6%</td>
</tr>
<tr>
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<td>36%</td>
<td>38%</td>
<td>42%</td>
</tr>
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<td>9%</td>
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(n=72) 1979-1990
(n=116) 1991-2000
(n=168) 2001-2005
(n=218) 2006-2010
(n=257) 2011-2015
Surgical treatment of perihilar cholangiocarcinoma

Details of 54 octogenarians who underwent resection

- Bile duct resection alone
- Major Hx.
- Major Hx. + PD
- Major Hx. + PV
- Major Hx. + HA
- Major Hx. + PV • HA

Age distribution:
- 80
- 81
- 82
- 83
- 84
- 85
- 86
- 87
- 88
- 89
Details of 54 octogenarians who underwent resection

- Bile duct resection alone
- Major Hx.
- Major Hx. + PD
- Major Hx. + PV
- Major Hx. + HA
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Age

80 81 82 83 84 85 86 87 88 89
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- Bile duct resection alone
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Surgical treatment of perihilar cholangiocarcinoma
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Age

- 80
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89
Surgical treatment of perihilar cholangiocarcinoma

Details of 54 octogenarians who underwent resection

- Bile duct resection alone
- Major Hx.
- Major Hx. + PD
- Major Hx. + PV
- Major Hx. + HA
- Major Hx. + PV•HA

Died of aspiration pneumonia on day 29
Survival of 54 octogenarians who underwent resection

Survival rates:
- Disease-specific survival: 55%
- Overall survival: 42%
Conclusion

- Nearly 80% of patients are candidates of surgical resection.
- Most of locally advanced tumor can be resected using extended resection including trisectionectomy, vascular resection, and HPD.
- Resection is of value even in patients with node metastasis, or R1/2 resection.
- From viewpoint of liver function, patients with ICGK-F > 0.04 are candidates of resection. To get volume gain of the future remnant liver, PVE is useful. ALPPS is contraindicated.
- Elderly patients should not be precluded from surgery solely due to age.
Thank you for your attention