TACE for Portal Vein Thrombosis in HCC

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HCC: Prognostic Factors

- Liver function
- Tumor stage (extent)
- Angioinvasion
PVT in HCC

- **Prevalence**
  - 12.5~39.7% of patients

- **Prognosis**
  - Median survival if untreated: 2.7~4 months
PVT in HCC

PVT in HCC Causes:

- Rapid tumor spread
- Portal hypertension
- Deterioration of hepatic function
- Infiltrative tumor growth
- Associated arterioporal shunt
PVT in HCC:
Treatment Options

- Intraarterial infusion chemotherapy
- IAC + Systemic interferon-alpha
- TACE
- TACE + Radiotherapy
- (TACE) + Surgery + (TACE or IAC)

→ No consensus!!
TACE for HCC with PVT

- Considered as a contraindication
  - Potential risk of ischemic liver damage $\rightarrow$ hepatic insufficiency
- TACE is safe if hepatic functional reserve is good.

TACE for HCC with PVT

  - Median survival 6 months
  - Cumulative survival rate
    - 48%(6m), 30%(1y), 18%(2y), 9%(3y)

- Georqiades CS et al (2005, JVIR)
  - Median survival 9.5 months
  - Cumulative survival rate
    - 60%(6m), 25%(1y), 12.5%(1.5y)
### TACE in PVT: Favorable Responders

(N = 31)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good liver function (Child class A)</td>
<td>28</td>
</tr>
<tr>
<td>Localized (nodular) primary tumor</td>
<td>22</td>
</tr>
<tr>
<td>Compact retention of Lipiodol in tumor thrombi</td>
<td>5</td>
</tr>
<tr>
<td>Regression of portal tumor thrombi</td>
<td>15</td>
</tr>
</tbody>
</table>

TACE in PVT: Long-term Survival

Group I (extensive)

Group II (localized)

\[ p = 0.0001 \text{ (Wilcoxon)} \]

50/M, PVT with APS

- G/M/A(2000/4mg/30mg) + L/A(4/30)

7Yr survival
54/M: Diffuse HCC & PV Thrombosis

95-12-28
F/U Studies: Complete Remission
PVT in HCC: Prognostic Factors

- Hepatic functional reserve
- PVT extent
- Primary parenchymal tumor
- Treatment response
Technical Problems of TACE in PVT

- Arterioportal shunt
- Fine arterial network supplying PVT
  - Difficult to control PV tumor thrombi
PVT & APS in HCC: TAE/TACE

- Sandwich technique
  - Gelfoam + anticancer drugs
  - L/A emulsion
- Glue embolization
- Absolute ethanol
60/M, AJN, Hematemesis: Glue+Gelf/Adr Embolization

1999-08-27

1999-11-09

2002-04-06
Natural History of PVTT

- Child A
- N=47 (31 TACE, 16 untreated controls)
- Median survival time (150 vs 90 days)

The Safety and Efficacy of Transcatheter Arterial Chemoembolization in the Treatment of Patients with Hepatocellular Carcinoma and Main Portal Vein Obstruction

A Prospective Controlled Study

Additional superselective intraarterial infusion of a chemotherapeutic agent (CDDP) after conventional TACE may allow its delivery in full strength to the residual small tumor feeders, which can lead to better treatment response of portal tumor thrombi and longer survival of the patients.
Hypothesis: CDDP-TACE
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Hypothesis: CDDP-TACE

- Iodized oil
- Gelatin sponge
- CDDP

C-TACE + CDDP
Purpose

To evaluate retrospectively whether CDDP-TACE can improve the survival of the patient with HCC with PVTT
Materials and Methods

- **Inclusion criteria**
  - HCC associated with PVTT
  - Child-Pugh score 5

- **77 consecutive patients**
  - 5 patients excluded
    - 2: liver transplantation imm. after TACE
    - 4: combined radiation Tx. for PVTT

- **Study population**
  - 71 patients
    - 32 to 74 years (median, 52 years)
    - Tumor ranged from 2.0 cm to 16.0 cm (median; 8.9 cm)
Materials and Methods

- **Group I (n=40):** c-TACE
  - Iodized oil-doxorubicin HCl emulsion and gelatin sponge particles

- **Group II (n=31):** c-TACE + CDDP
  - Dose of CDDP: 70-100mg (1mg/m)
Materials and Methods

- Analysis of Prognostic factors (n=29)
  - 13 baseline patient factors
    - age, sex, performance status, portal hypertension, hepatitis B and C infection, AST, ALT, ALP, serum albumin, serum total bilirubin levels, platelet count, prothrombin time
  - 14 baseline tumor factors
    - serum α-fetoprotein level, tumor location (unilobar vs bilobar), tumor multiplicity, diffuse type of tumor, primary tumor size, primary tumor extent (>50%), tumor hypervascularity, completeness of PV trunk occlusion, combined HV or IVC thrombosis, LN invasion, extrahepatic tumor invasion, previous TACE, additional systemic chemotherapy
  - 2 procedure-related factors
    - additional CDDP infusion
    - procedure time later than July 1, 2003
Materials and Methods

- Statistical analysis
  1. Uni- and Multivariate analysis for the potential prognostic factors using Cox proportional hazard model
  2. Comparability check for the two groups using chi-square test
  3. Comparison of overall survival rates between the two groups using Kaplan-Meier estimation
Results: Univariate Analysis

- Five significant factors
  - Serum AST level >80 units/L  \( (P=0.000) \)
  - Serum ALP level >150 units/L  \( (P=0.008) \)
  - Primary tumor >50%  \( (P=0.005) \)
  - Additional CDDP infusion  \( (P=0.000) \)
  - Time factor (later than July 1, 2003)  \( (P=0.001) \)
Results: Multivariate Analysis

- Only two independently significant factors.
  - Serum AST level >80 units/L ($P=0.007$)
  - Additional CDDP infusion ($P=0.000$)

- Serum ALP level, primary tumor extent, time factor
  - $P=0.148, 0.137, \text{ and } 0.997$, respectively

<table>
<thead>
<tr>
<th>Variables</th>
<th>Regression coefficient</th>
<th>Standard error</th>
<th>Hazard ratio</th>
<th>$P$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum AST level &gt;80 units/L</td>
<td>0.776</td>
<td>0.290</td>
<td>2.174 (1.231-3.840)</td>
<td>0.007*</td>
</tr>
<tr>
<td>Additional CDDP infusion</td>
<td>-0.528</td>
<td>0.150</td>
<td>0.590 (0.439-0.792)</td>
<td>0.000*</td>
</tr>
</tbody>
</table>

*:Statistically significant ($p$-value<0.05)
Results: Subgroup Analysis

- In Group I
  - Serum AST level was the only significant factor ($P=0.021$)

- In Group II
  - Primary tumor extent was the only significant factor ($P=0.0361$)
## Results: Comparability

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
<th>Odds Ratio</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥ 52 years</td>
<td>24</td>
<td>11</td>
<td>0.367 (0.139–0.968)</td>
<td>0.040*</td>
</tr>
<tr>
<td>Performance status score (0/ 1–2)</td>
<td>29</td>
<td>18</td>
<td>0.525 (0.194–1.421)</td>
<td>0.202</td>
</tr>
<tr>
<td>Serum albumin level &lt;3.8mg/dL</td>
<td>19</td>
<td>9</td>
<td>0.452 (0.167–1.221)</td>
<td>0.114</td>
</tr>
<tr>
<td>Serum AST* level &gt;80 units/L</td>
<td>25</td>
<td>12</td>
<td>0.379 (0.144–0.995)</td>
<td>0.085</td>
</tr>
<tr>
<td>Platelet count &lt;100,000(×10⁹/L)</td>
<td>7</td>
<td>7</td>
<td>1.375 (0.426–4.440)</td>
<td>0.594</td>
</tr>
<tr>
<td>Portal hypertension (no/ yes)</td>
<td>26</td>
<td>27</td>
<td>3.635 (1.057–12.50)</td>
<td>0.034*</td>
</tr>
<tr>
<td>Serum α-fetoprotein &gt;1000ng/mL</td>
<td>19</td>
<td>19</td>
<td>1.750 (0.675–4.537)</td>
<td>0.248</td>
</tr>
<tr>
<td>Tumor location (unilobar / bilobar)</td>
<td>26</td>
<td>21</td>
<td>1.131 (0.418–3.057)</td>
<td>0.809</td>
</tr>
<tr>
<td>Tumor multiplicity (single/ multiple)</td>
<td>2</td>
<td>0</td>
<td>1.815 (1.466–2.247)</td>
<td>0.207</td>
</tr>
<tr>
<td>Tumor size (≤5cm / &gt;5cm)</td>
<td>31</td>
<td>25</td>
<td>1.210 (0.379–3.857)</td>
<td>0.747</td>
</tr>
<tr>
<td>Diffuse tumor type</td>
<td>16</td>
<td>10</td>
<td>0.714 (0.267–1.910)</td>
<td>0.502</td>
</tr>
<tr>
<td>Primary tumor extent &gt;50% (no/ yes)</td>
<td>12</td>
<td>5</td>
<td>0.449 (0.139–1.449)</td>
<td>0.174</td>
</tr>
<tr>
<td>Portal vein trunk occlusion (partial / complete)</td>
<td>17</td>
<td>23</td>
<td>3.890 (1.403–10.79)</td>
<td>0.008*</td>
</tr>
<tr>
<td>Combined inferior vena cava thrombosis</td>
<td>5</td>
<td>5</td>
<td>1.346 (0.353–5.138)</td>
<td>0.663</td>
</tr>
</tbody>
</table>
Results: Survival

- Median survival time: 25 weeks vs 67 weeks
- One-, two-, three-year estimated survival rate
  - Group I – 20.6%, 5.1%, 2.6%, Group II – 58.7%, 43.0%, 17.9%
  - Difference between two groups was statistically significant (p=0.0001)
Results: Survival

- One-, two-, three, four-year estimated survival rate
  - Improved PVTT: 80.0%, 63.0%, 26.3%, 26.3%
  - Stable or progressive PVTT: 14.3%, 0.0%

Difference between two groups was statistically significant (p=0.0000).
Results: Survival

- One-, two-, three, four-year estimated survival rate
  - Before July 1, 2003: 50.1%, 36.4%, 13.6%, 13.6%
  - After July 1, 2003: 17.9%, 0.0%
  - Difference between two groups was statistically significant (p=0.0004)
Results: Complications

- **Major complication rate**: 2.8% (2/71)
  - All in non-CDDP infusion group
  - One progressive hepatic failure after TACE
    - dead 11 weeks after initial TACE
  - One Listeria sepsis
    - recovered after conservative management

- **Permanent conversion into B class**
  - Five patients (4 in Group I, 1 in Group II)
  - One-, two-, three, four-year survival rate
    - 100%, 100%, 50%, 50%
Results

- **Complete remission**
  - No viable tumor (incl. PVTT) on CT
  - No tumor stain on angio
  - Normal(normalized) AFP
  - No new lesion for at least 6 months
- **9 CR**
  - All in Group II
  - 8/9 patients still alive
Case 1. M/33, Initial CT
Case 1. M/33, 1st TACE
Case 1. M/33, 1\textsuperscript{st} TACE

L/A mixture, Gelfoam infusion via S4, LHA, RHA feeders
Case 1. M/33, 1st TACE

Additional CDDP infusion after decreased blood flow

- S4 (10mg)
- LHA (20mg)
- RHA (70mg)
Case 1. M/33, 1st TACE

Residual tumor staining
L/A mixture, gelfoam infusion via S4, RHA feeders
CDDP infusion via S4(30mg), RHA(40mg)
Case 1. M/33, 2nd TACE

small tumor staining of left PV thrombus supplied by S4 artery
Case 1. M/33, 3rd TACE
Case 1. M/33, 1yr F/U: CR
Case 2: M/39, CDDP infusion, 20mg at RIPA / 40mg at RH, before embolization, 40 mg at RH, after embolization.

Initial CT

Initial TACE
Case 2: M/39, CDDP infusion, 20mg at RIPA / 40mg at RH, before embolization, 40 mg at RH, after embolization
Case 2: M/39, CDDP infusion, 20mg at RIPA / 40mg at RH, before embolization, 40 mg at RH, after embolization
Conclusion

- Prognosis of HCC with MPVT after c-TACE
  - Child-Pugh score A5
  - 1Y-SR: 18%

- Additional CDDP (cisplatin) infusion after conventional TACE (incl. superselective catheterization of PVTT feeders)
  - CR in 32% of patients
  - 3-, 4Y-SR: 18%
  - Prognostic factor
    - Primary tumor extent
    - Treatment response
Thank you.