Peritonectomy, Perioperative and Intraoperative Intraperitoneal Chemotherapy for Carcinosis Arising from Gastric Cancer

Results of a French Multicentric Analysis

6th IWPSM Lyon 17th-19th 2008
Retrospective study
1344 procedures-1290 patients
- HIPEC : 1154 cases (86%)
  - Open abdomen : 726 cases
  - Closed abdomen : 391 cases
- EPIC : 190 cases (14%)
25 centers
French: 20, Swiss: 1, Canadian : 2, Belgium : 2
Study of the short term and long term results, mortality, morbidity
Prognostic factors
Indications
Report “carcinomatosis arising from gastric cancer”

French Association for Surgery (AFC)

Main etiology

<table>
<thead>
<tr>
<th>Etiology</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer colo-rectal</td>
<td>523</td>
<td>40,5</td>
</tr>
<tr>
<td>Pseudomyxome péritonéal</td>
<td>301</td>
<td>23,3</td>
</tr>
<tr>
<td><strong>Estomac</strong></td>
<td>159</td>
<td>12,3</td>
</tr>
<tr>
<td>Mésothéliome péritonéal</td>
<td>88</td>
<td>6,8</td>
</tr>
<tr>
<td>Adénocarcinome appendiculaire</td>
<td>50</td>
<td>3,9</td>
</tr>
<tr>
<td>Adénocarcinome du grêle</td>
<td>45</td>
<td>3,5</td>
</tr>
<tr>
<td>Carcinome séreux primitif péritonéal</td>
<td>33</td>
<td>2,5</td>
</tr>
<tr>
<td>Sarcomatose</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>Autres</td>
<td>66</td>
<td></td>
</tr>
</tbody>
</table>

6th IWPSM
Lyon
17th-19th 2008
Gastric cancer: 2\textsuperscript{nd} rank mortality by cancer in the world (> 600 000 deaths/year)

\textit{Incidence of gastric cancer in males} (Crew et al W J Gastroenterol 2006)

- Carcinomatosis: present among 75\% of the patients that died from gastric cancer (Roviello F et al Br J Surg 2003)
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- 159 patients with gastric cancer and PC
- 15 centers
- M: 83  F: 76
- Mean age 53.4 ± 12.8
- PC Synchronous : 44%
- PC Metachronous : 66%

1344 procedures
- F: 56%  M: 44%
- Mean age : 52 ± 12
- Synchronous resection of the primitive tumor : 32.5%

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159 cases - **French Association for Surgery (AFC)**

- **Histology:**
  - Adenocarcinoma well differentiated: 22.5%
  - Adenocarcinoma differentiated: 20%
  - Adenocarcinoma poorly differentiated: 57.5%

*6th IWPSM Lyon 17th-19th 2008*
Clinical presentation:
- Laparotomy for other etiology than carcinomatosis: 35%
- Abdominal pain: 21%
- CT scan: 14.5%
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Intraoperative data
- CCR-0: 56%
- CCR-1 (<2,5mm): 25%
- CCR-2/3(>2,5mm): 19%

1344 procedures
- CCR-0: 75%
- CCR-1 (<2,5mm): 16%
- CCR-2(>2,5mm): 8%

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**Intraoperative data**

- HIPEC : 154 cases (94%)
  - Closed abdomen : 142 cases (54%)
  - Open abdomen : 46%
- EPIC : 12 cases (7.5%)
- Mitomycin C : 83%
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159 cases French Association for Surgery (AFC)

Mortality-Morbidity of procedures

- Mortality: 10 cases (6.5%)
- Morbidity grade 3-4: 38 cases (27.8%)
  - Digestive fistula: 16%
  - Relaparotomy: 14%
  - Mean post-operative stay: 24.2±19 days

1344 procedures

- Mortality: 4.1%
- Morbidity gr. 3-4: 33.8%
  - Dig. fistula: 9.6%
  - Relaparotomy: 14%
  - Mean post-operative stay: 24.1±18 days
Report “Carcinomatosis arising from gastric cancer” 159 cases - French Association for Surgery (AFC)

- Difference of morbidity-mortality within 30 days
  - According to center (p<0.0001)
  - If age > 61 years: 44% vs 30% (p = 0.06)
  - If EPIC: 60% vs 29% (p=0.051)

1344 procedures
- Centers >11 years experience 25% p < 0.0001
- If age > 61 years: 39% vs 33% (p=0.07)
- If EPIC: (41% vs 33%) (p=0.03)
Report “Carcinomatosis arising from gastric cancer”

French Association for Surgery (AFC)

- No difference of morbidity-mortality within 30 days of peritonectomy-chemotherapy
  - According to Stage
    - Gilly 0-1-2 : 33%
    - Gilly 3-4 : 21%
  - According to systemic preoperative chemotherapy
    - Yes : 24%
    - No : 36%
  - According to technique
    - Closed abdomen : 27%
    - Open abdomen : 29%
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French Association for Surgery (AFC)

Survival results, recurrences and prognostic study

- 7 lost of view (4.4%)
- Mean Survival: 7 months
- Survival 1, 3, 5 yr: 43%, 18%, 14%

Survival without recurrence at 3 yrs: 12%
Report “Carcinomatosis arising from gastric cancer”

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Significant difference (p=0.07) for Gilly’s stage (p=0.004, UA), and PCI Sugarbaker (p<0.001, UA). Survival results, recurrences and prognostic study. Survival with CCR (p<0.001, UA + MA).
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- Neo-adjuvant systemic chemotherapy
  - 1 year survival: 52 months vs 38 months
  - 5 years survival: 25 months vs 14 months (p=0.018 UA)

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Subgroup : total resection CCR-0 (85 patients)

Sugarbaker PCI main independent prognostic factor
(p<0,001 UA, p=0,038 MA)
## Discussion: Mortality and Morbidity

<table>
<thead>
<tr>
<th>Studies</th>
<th>N</th>
<th>Technique</th>
<th>Mortalité</th>
<th>Morbidité</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yonemura, Fujimura et al</td>
<td>83</td>
<td>Expander MMC+ CDDP</td>
<td>1%</td>
<td>7%? 3 fistulas</td>
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<tr>
<td>Surgery 1996</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Hall et al J Gastro Intest Surg 2004</td>
<td>34</td>
<td>HPEC/Close MMC</td>
<td>3%</td>
<td>35% 4 fistulas</td>
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<tr>
<td>Glehen et al arch Surg 2004</td>
<td>46</td>
<td>HPEC/Close MMC</td>
<td>4%</td>
<td>27% 6 fistulas 4 ré-interventions</td>
</tr>
<tr>
<td>AFC</td>
<td>159</td>
<td>HIPEC Open/close</td>
<td>6%</td>
<td>28% 24 fistulas</td>
</tr>
</tbody>
</table>

AFC: Abdominal Federal Center
Prospective study

- 1989-2000; 49 patients <70 years
- HIPEC
  - 28 synchronous gastrectomy
  - 21 post gastrectomy (mean delay HIPEC: 30 days)

- 1 year survival: 48% (Stade I,II: 71% - R0,R1: 75%)
- 5 years survival: 16% (Stade I,II: 30% - R0,R1: 29%)

- 4 patients without recurrence at 8, 9, 9, 11 years
  - All R0
  - All Gilly 1
### Others Results of HIPEC in gastric cancer: Asiatic studies

1 year survival: 30-60%
5 years survival: 10-30%

<table>
<thead>
<tr>
<th>Reference</th>
<th>Location</th>
<th>Treatment (patients)</th>
<th>Survival %</th>
<th>Survival years</th>
<th>Survival (median) months</th>
<th>P-value</th>
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</thead>
<tbody>
<tr>
<td>Fujimoto et al. [59]</td>
<td>Chiba</td>
<td>IP chemo (30)(^a)</td>
<td>80.4</td>
<td>1</td>
<td>n.a.</td>
<td>&lt;0.001</td>
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<td>Hist control (29)(^a)</td>
<td>34.2</td>
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<td>n.a.</td>
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<td>IP chemo (20)</td>
<td>78.0</td>
<td>1</td>
<td>n.a.</td>
<td>&lt;0.001</td>
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<td>Hist control (7)</td>
<td>0.0</td>
<td></td>
<td>n.a.</td>
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<tr>
<td>Yonemura et al. [61]</td>
<td>Kanazawa</td>
<td>IP chemo (41)</td>
<td>28.5</td>
<td>3</td>
<td>n.a.</td>
<td>n.a.</td>
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<tr>
<td>Yonemura et al. [62]</td>
<td>Kanazawa</td>
<td>IP chemo (32)</td>
<td>55.0</td>
<td>3</td>
<td>n.a.</td>
<td>&lt; 0.001</td>
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<td>Rand control (35)</td>
<td>7.0</td>
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<td>n.a.</td>
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<tr>
<td>Yonemura et al. [65]</td>
<td>Kanazawa</td>
<td>IP chemo (83)(^a)</td>
<td>11.0</td>
<td>5</td>
<td>n.a.</td>
<td>n.a.</td>
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<tr>
<td>Yu et al. [23]</td>
<td>Taegu</td>
<td>IP chemo (33)(^a)</td>
<td>33.0</td>
<td>n.a.</td>
<td>2.78</td>
<td>0.0098</td>
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<tr>
<td></td>
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<td>Rand control (31)(^a)</td>
<td>31.0</td>
<td>n.a.</td>
<td>4.9</td>
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<tr>
<td>Hirose et al. [66]</td>
<td>Fukui</td>
<td>IP chemo (32)</td>
<td>n.a.</td>
<td>n.a.</td>
<td>11.0</td>
<td>0.0479</td>
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<tr>
<td></td>
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<td>Hist control (20)</td>
<td>n.a.</td>
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<td>6.0</td>
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<td>Yoo et al. [54]</td>
<td>Seoul</td>
<td>IP chemo (91)(^a)</td>
<td>17.3</td>
<td>3</td>
<td>n.a.</td>
<td>&lt;0.0000</td>
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<td>Hist control (140)(^a)</td>
<td>11.0</td>
<td></td>
<td>n.a.</td>
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</tr>
</tbody>
</table>

n.a., not available; hist, historical; rand, randomized; IP chemo, intraperitoneal chemotherapy.

\(^a\)Includes other patients with stage IV disease.
Role of HIPEC to prevent recurrence after curative gastrectomy?


- 1987-1996 Peritoneal recurrence
- 141 gastric cancer HIPEC: 19/71
- Survival: 1-4-8 years Control: 33/70
  - HIPEC: 88-76-62%
  - Control Group: 77-58-49%

Comparison of survival between the T3 (p = 0.0379)

Original article

A controlled clinical study of serosa-invasive gastric carcinoma patients who underwent surgery plus intraperitoneal hyperthermo-chemo-perfusion (IHCP)

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Conclusion

- Post operative mortality is high for patients treated for carcinomatosis of gastric origin, especially for patients aged 60 and more.
- The treatment of carcinomatosis from gastric cancer by peritonectomy and HIPEC has worse long term results than the treatment of carcinomatosis from others causes.
- Long survival after peritonectomy and HIPEC for carcinomatosis arising from gastric cancer are possible if the extension of the carcinosis is low and the resection R0.
The future

- Fact that survival is better among patients that had neo-adjuvant chemotherapy.
- Need of trials with others molecules than MMC.
- Role of HIPEC as an adjuvant therapy deserves to be studied in a randomized multicentric trial.
Carcinoses péritonéales d’origine digestive et primitive
Report 110th French Congress of Surgery
Paris October 1-3 2008

K ABOUD, C ARVIEUX, A ARVIN-BEROD,
D BENCHIMOL, E BENIZERI, JM BERREDER,
JL BERNARD, J BONASTRE, N BOSSARD,
A BOSCHETTO, F BOUTITIE, C BRIGAND,
N CARLIN, E COTTE, S DAGOIS, P DUBE,
D ELIAS, C EVENO, G FERRON, P GERTSH,
FN GILLY, O GLEHEN, D GOERE, J HABRE,
B KARIMDJEE-SOHILI, G LAVAL,
G LORIMIER, R LOUGNARATH,
B MANSVELT, F MARCHAL, J MATEO,
P MEEUS, JP MESTRALLET, C MEYER, S
MSIKA, JC OLLIER, G PANGOS, M POCARD,
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P RAT, C REBISCHUNG, S ROHR,
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JJ TUECH, O TURRINI, O VAN DER
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