Pelvic Peritonectomy without Intraperitoneal Chemotherapy for Localized Peritoneal Carcinomatosis

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Abstract. Aim: This study assessed the feasibility of pelvic peritonectomy for carcinomatosis localized in the pelvic cavity. The survival and clinical benefits were examined, especially in colorectal cancer. Patients and Methods: Seventeen patients underwent pelvic peritoneal resection for peritoneal dissemination localized in the pelvis (10 colorectal, six ovarian, one cervical cancer). The male/female ratio was 5/12. The age range was 31-83 (median=63) years. The peritoneal cancer index was 2-16 (median=4). Perioperative intraperitoneal chemotherapy was not performed. Results: For all 17 cases, pelvic exenteration significantly increased invasiveness in the treatment of pelvic peritoneal carcinomatosis (p<0.05). Additionally, pelvic exenteration did not improve prognosis. In all cases, the serum carcinoembryonic antigen (CEA) levels decreased significantly from a mean of 15.1 (range=0.8-55.7) to 2.4 (range= 0.5-7.4) ng/ml (paired t-test, p<0.05). For colorectal cancer, serum CEA decreased significantly from 19.3 (range=1.2-55.7) to 2.7 (range=0.5-7.4) ng/ml (paired t-test, p<0.05). In the colorectal cancer series, cumulative 1- and 3-year overall survival rates were 89% and 71%, respectively. One- and 3-year recurrence-free survival rates were 78% and 67%, respectively. Conclusion: The cytoreductive effect of this method is feasible and excellent for pelvic carcinomatosis. Pelvic peritonectomy without perioperative intraperitoneal chemotherapy is a safe, effective procedure for peritoneal carcinomatosis from colorectal cancer localized in the pelvis.

The presence of peritoneal metastasis is one of the most important prognostic factors in gastrointestinal, as well as gynecological malignancies. Peritoneal carcinomatosis arising from colorectal cancer has been considered a terminal condition without curative treatment options. The prognostic study of Chu et al. (1) in 1989 reported on 45 patients with a median survival of 6 months after treatment with fluorouracil and leucovorin.

According to Jacquet and Sugarbaker (2), peritoneal carcinomatosis is evaluated by the peritoneal carcinomatosis index (PCI). This assessment combines lesion size (LS) (0: no macroscopic tumor; 1: tumor <0.5 cm; 2: tumor 0.5-5 cm; and LS3: tumor >5 cm) with tumor distribution (abdominopelvic region 0-12) to quantify the disease as a numerical score (PCI=0-39). They reported that peritonectomy and intraoperative chemohyperthermic peritoneal perfusion are necessary for improving the prognosis of peritoneal carcinomatosis.

Peritonectomy and perioperative intraperitoneal chemotherapy with hyperthermia is one of the best modalities for peritoneal carcinomatosis from colorectal cancer. However, life-threatening complications sometimes occur with such therapy.

Completeness of cytoreduction (CCR) is important for any effectiveness of chemohyperthermic peritoneal perfusion. Recently, some reports emphasized that improved prognosis is only achieved by the inclusion of oxaliplatin (3). Occasionally, peritoneal carcinomatosis is localized in the pelvic cavity due to gravity. We hypothesized that pelvic peritonectomy is a curative method for peritoneal carcinomatosis, which is limited to the superficial pelvic peritoneum, avoiding intraperitoneal chemotherapy. Pelvic peritonectomy is tumor resection with peritoneal peeling of the pelvic space, avoiding combined resection of adjacent organs, enabling postoperative dead space to be minimized. Dead space will cause residual abscess and delay in adjuvant chemotherapy. Pelvic peritonectomy aims at R0 resection.
and needs combined resection of the rectum with or without seminal vesicles for males (Figure 1A). Additionally, combined resection of the ovaries and/or uterus is sometimes needed for females (Figure 1B).

The present study was specifically designed to assess the safety of pelvic peritonectomy for carcinomatosis localized in the pelvic cavity; the survival and clinical benefits were examined, especially in colorectal cancer.

Patients and Methods

Seventeen patients underwent pelvic peritoneal resection, with 15 synchronous and 2 metachronous peritoneal disseminated tumors localized in the pelvis without extra-abdominal distant metastasis. The male/female ratio was 5/12. The age range was from 31 to 83 (median= 63) years. The PCI ranged between 2 and16 (median=4). Patients operated on and enrolled in this study had colorectal cancer (=10), ovarian cancer (=6), and cervical cancer (=1). Primary locations of colorectal cancer were the sigmoid colon (=6), rectum (=3) and transverse colon (=1). In colorectal cancer, lymph node dissection was D3/D2/D1=3/4/3. Concerning the operative procedures, there were six lower anterior resections, one abdominoperineal resection, one Hartmann’s procedure, and nine pelvic exenterations (PE). Tumor stage and histology were evaluated by the TNM Classification of Malignant Tumors (4).

All cytoreductive procedures were performed by or under supervision of a single surgeon (TS). Perioperative intraperitoneal chemotherapy was not performed in any case.

Statistical analysis. The Mann–Whitney U-test was used for the comparison of differences in means of discrete variables. For comparison of serum tumor marker levels, paired t-test was used. Analysis of overall survival and recurrence rate were performed using the Kaplan–Meier method and were compared using the log-rank test. These statistical analyses were performed using SPSS (Ver. 11; Chicago, IL, USA). A significant difference was assumed for p<0.05.

Results

Descriptive data. The median hospital stay was 18 (range 9-46) days. The median operative time was 322 (range=229-866) min. The median blood loss was 755 (range=100-9022) ml. Postoperatively, the first flatus was passed at day 2 (median), and the first meal at day 3 (median). Postoperative complications occurred in six patients; in these, major morbidity was observed in one.

The most frequent complications were wound infection without hematological toxicity in 2 patients. No re-operations were needed and the mortality rate was 0. Histopathological type was as follows: three well-differentiated adenocarcinomas, four moderately-differentiated adenocarcinomas, two mucinous adenocarcinomas, and one poorly-differentiated adenocarcinoma in colorectal cancer; four endometrioid adenocarcinomas and one poorly-differentiated adenocarcinoma in ovarian cancer; and one endocervical-type adenocarcinoma in cervical cancer. Intraoperative peritoneal lavage cytology was performed in 14 cases at the survey of the peritoneal cavity after laparotomy, before tumor resection. The results disclosed that there were six positive cases and eight negative cases. Tumor characteristics in the colorectal cancer series are shown in Table I. According to the TNM classification, T-factor was T4/T3=6/4, and N factor was N2/N1/N0=4/1/5. PCI ranged from 2 to 16 (median=4). Cytoreductive surgery was: two CCR1 and eight CCR0.

Pelvic exenteration. PE was additionally needed for R0 resection in nine cases. Operative time and blood loss were significantly greater in PE cases than in non-PE cases by the Mann–Whitney U-test (median: 272 min vs. 361 min; 231 ml vs. 1812 ml, p<0.005) (Figure 2A, 2B). Postoperative hospital stay was significantly longer in PE cases than in non-PE cases.

<table>
<thead>
<tr>
<th>Case</th>
<th>Peritoneal cancer index</th>
<th>Size of primary tumor (cm)</th>
<th>Histology*</th>
<th>pT</th>
<th>pN</th>
<th>Lymphatic invasion</th>
<th>Venous invasion</th>
<th>Peritoneal lavage cytology</th>
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<td>p</td>
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</tr>
<tr>
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<td>4</td>
<td>9x7.5</td>
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<td>p</td>
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<td>p</td>
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</tbody>
</table>

*According to UICC classification (4); Well: well-differentiated adenocarcinoma; mod: moderately-differentiated adenocarcinoma; muc: mucinous adenocarcinoma; poor: poorly-differentiated adenocarcinoma; p: positive; n: negative; N/A: not available.
cases, by the Mann–Whitney U-test (median: 9 days vs. 20 days, \( p < 0.05 \)) (Figure 2C). For all cases, PE significantly increased invasiveness in the treatment of pelvic peritoneal carcinomatosis (\( p < 0.05 \)). The recurrence curves estimated by Kaplan–Meier method showed the recurrent status of PE-performed cases was significantly poorer than in non-PE-performed cases (log-rank test, \( p < 0.05 \)) (Figure 3). PE did not improve the prognosis.

**Cytoreductive effect.** For all cases, pre- and postoperative average serum CEA levels were 15.1 (range=0.8-55.7) and 2.4 (range=0.5-7.4) ng/ml, respectively. After pelvic peritonectomy, serum CEA decreased significantly (paired \( t \)-test, \( p < 0.05 \)). The average pre- and postoperative serum CA19-9 levels were 115 (range=1-1152) and 10 (range=2-28) U/ml, respectively. The change of serum CEA levels indicates that the cytoreductive effect was excellent.

**Adjuvant chemotherapy.** For the colorectal cancer series, eight cases underwent adjuvant chemotherapy. Oral administration of 5-fluorouracil and leucovorin was performed for one case. FOLFOX, an intravenous administration of 5-fluorouracil, leucovorin, and oxaliplatin, was performed for seven cases.

**Survival data.** At the last follow-up visit, 16 patients were available for survival analysis whereas one patient was lost to follow-up.

In the colorectal cancer series, the survival curves estimated by the Kaplan–Meier method showed that cumulative 1- and 3-year overall survival rates were 89% and 71%, respectively.
One- and 3-year recurrence-free survival rates were 78% and 67%, respectively (Figure 4A).

**Discussion**

Peritoneal metastasis is one of the most important prognostic factors for gastrointestinal and gynecological malignancies. Peritoneal carcinomatosis can develop without distant metastasis (5). The cytoressive effect of pelvic peritonectomy was excellent in this study. On the other hand, PE increases invasiveness while its benefit is still controversial. In this study, for pelvic peritoneal carcinomatosis, PE did not improve the prognosis. Taking its invasiveness into consideration, stripping of the pelvic peritoneum might be effective for the treatment of localized peritoneal carcinomatosis.

Thirty percent of patients with colorectal adenocarcinoma disease progression eventually develop synchronous (8-10%) or metachronous colorectal peritoneal carcinomatosis (25%) (6, 7). According to Glehen et al., the morbidity rate is 22.9% and mortality rate is 4% after cytoreductive surgery and perioperative intraperitoneal chemotherapy (8). Life-threatening complications sometimes occur in such therapy. Therefore, peritonectomy and perioperative intraperitoneal
chemotherapy with hyperthermia is not recommended for general hospitals. The survival rate after cytoreductive surgery is still reported to be unsatisfactory (8). A multinational registry from 28 international treatment centers demonstrated that the median survival was 19 months and the 3-year survival was 39%, in 506 patients with colorectal peritoneal carcinomatosis who were treated with cytoreductive surgery and perioperative intraperitoneal chemotherapy (8).

Many studies identified that patients undergoing complete cytoreduction had an improved prognosis, achieving a median survival of 28 to 60 months and 5-year survival of 22% to 49% (8-13). Similarly to primary colorectal cancer surgery or nearly all surgical oncology cases, if complete resection cannot be achieved, long-term survival is not probable. Therefore, it is important to be able to select those patients who are likely to benefit from this intervention. Systemic adjuvant chemotherapy might improve the tumor status, whereas local control could be improved by surgery. The serum CEA levels is a prognostic indicator of colorectal cancers (14) and they decreased postoperatively in this study.

Pelvic peritonectomy is feasible for colorectal cancer with peritoneal carcinomatosis. Avoiding combined resection to adjacent organs, postoperative dead space can be minimized. Dead space will cause residual abscess and delay in adjuvant chemotherapy. This method is simple without life-threatening complications and very simple without perioperative intraperitoneal chemotherapy. In this decade, FOLFOX improved the prognosis of patients with colorectal peritoneal carcinomatosis (3). This approach is recommended for general hospitals as well as high-volume centers. This finding indicates that patients with superficial peritoneal carcinomatosis are good candidates for pelvic peritonectomy.

Pelvic peritoneal carcinomatosis from colorectal cancer should be treated as a loco-regional disease.

We can conclude that the cytoreductive effect of this method is feasible and excellent for pelvic carcinomatosis of colorectal and ovarian cancer.

Pelvic peritonectomy without perioperative intraperitoneal chemotherapy is a safe and effective procedure for peritoneal carcinomatosis from colorectal cancer, that is localized in the pelvic cavity.

To our knowledge, this concept is a novel and original operative procedure. However, the study data originated from a single institution. Therefore, more cumulative patients and further follow-up are necessary.
Conflicts of Interest

The Authors declare that they have no conflicts of interest related to the publication of this article.

Acknowledgements

We thank Michel Gagner, Herbert Wertheim School of Medicine, Florida International University, Miami, FL, USA, and Barry Salky, Mount Sinai Hospital, NY, USA, for assistance with preparation of this manuscript. The present theme was awarded the “Young Investigator Award 2012 of 6th Colorectal Disease Symposium in Tokyo”.

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Received December 11, 2012
Revised January 17, 2013
Accepted January 17, 2013