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Original research

Impacts of peritoneal cancer index on the survival outcomes of patients with colorectal peritoneal carcinomatosis

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HIGHLIGHTS

- This is a retrospective study of 168 patients with CRPC.
- Patients in low PCI groups had a lower major morbidity rate and a higher overall survival.
- Early referral to specialist centre is necessary.

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ABSTRACT

Introduction: Peritoneal cancer index (PCI) has been suggested to be the most important prognostic factors for the outcomes in colorectal peritoneal carcinomatosis (CRPC).
Methods: This was a retrospective study of prospectively collected data of 168 consecutive patients with CRPC following cytoreductive surgery (CRS) and perioperative intraperitoneal chemotherapy (PIC). Patients were divided into five groups according to their PCI.
Results: Hospital mortality was 0%. Patients in low PCI groups had a significantly lower major morbidity rate, shorter intensive care unit and high dependency unit stay and higher overall survival ($p=0.017$, 0.001, 0.046, $p<0.001$ respectively).
Conclusion: Combined CRS with PIC can be safely performed to provide encouraging survival benefits for patients with CRPC. Our findings suggest that this approach is particularly beneficial for patients with low volume of disease. Early referral to specialist centre for evaluation is warranted for better survival outcomes.

1. Introduction

Colorectal peritoneal carcinomatosis (CRPC) was considered as a rapidly fatal disease. Historically, the median survival of patients with CRPC was only six months with systemic chemotherapy with or without palliative surgery [24]. With evolving systemic chemotherapy, the median survival has improved to 13 months ranging from 5 to 24 months. However the 5-year survival of these patients after systemic chemotherapy is still poor and ranges from 0 to 22% [1,3,4,8,14,17,20,21,25,27,28,30,36].

In the last two decades, the combination of cytoreductive surgery (CRS) and perioperative intraperitoneal chemotherapy (PIC) have been developed rapidly and considered as an innovative technique for CRPC. PIC consists of hyperthermic intraperitoneal chemotherapy (HIPEC) and early postoperative intraperitoneal chemotherapy (EPIC). It has shown the encouraging survival benefits and is currently recommended as a standard treatment for CRPC in selected patients [10,18,36,38]. It has been shown that the extent of CRPC, measured by peritoneal cancer index (PCI), is the main prognostic factors [6,9,10,34]. Several studies have attempted to set a cut-off of PCI, beyond which CRS and PIC would be contraindicated [6,15,39,40]. However the proposed values were

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variable without any consensus. One recent study done by Faron (2015) demonstrated a perfect linear relationship between the PCI and overall survival [16]. The aim of this paper is to review clinical outcomes of patients with CRPC and determine the survival differences of patients with different PCI.

2. Patients and methods

2.1. Settings

This is a retrospective study of prospectively collected data of patients with CRPC, who underwent CRS and PIC by the same surgical team at St George hospital, Sydney, Australia between January 1996 and Oct 2015. All the clinical and treatment-related data were collected and entered into a computerised database in order to evaluate the perioperative outcomes of these patients. A signed informed consent was obtained from all patients.

2.2. Patients

Patients had a good performance status (World Health Organisation Performance Status $\leq$2), and had a histological diagnosis of CRPC. All patients were managed by a standard treatment protocol combining CRS and PIC. Suitability to undergo CRS and PIC was evaluated during a regular weekly meeting attended by a multidisciplinary team (MDT) including surgical oncologists, medical oncologists, radiologists, cancer care nurses and research staff. Exclusion criteria include synchronous liver metastases at the time of operation, debulking surgery (i.e. no PIC was given) or incomplete cytoreduction.

Patients were divided into six groups according to their PCI (Group I: PCI = 0; Group II: PCI 1–5; Group III: PCI 6–10; Group IV: PCI 11–15; Group V: PCI>15). Patients with negative pathology regardless of their PCI was categorised into group I (i.e. PCI = 0). Subgroup analysis was performed using the histological subtypes.

2.3. Preoperative management

All patients underwent standard preoperative investigations which included physical examination; double contrast-enhanced computed tomography (CT) scans of the chest, abdomen and pelvis; and CT portography or primovist magnetic resonance imaging of the liver. Positron emission tomography was performed in all patients in addition to the staging laparoscopy to assess the PCI if the scans showed borderline results.

Our current selection criteria for consideration of CRS and HIPEC included PCI $\leq$15, being able to perform complete cytoreduction, absence of extra-abdominal disease, no evidence of progressive disease in preoperative chemotherapy and no severe comorbidity.

2.4. CRS

An initial assessment of the volume and extent of disease was recorded using PCI. This assessment combines maximal diameter of lesion size (LS) (LS 0: no macroscopic tumour; LS 1: tumour <0.5 cm; LS 2: tumour 0.5–5 cm; and LS3: tumour >5 cm) with tumour distribution (abdominopelvic region 0-12) to quantify the extent of disease as a numerical score (PCI 0–39). CRS was performed using Sugarbaker's technique [35].

All sites and volumes of residual disease following CRS were recorded prospectively using CC score (CC0-no macroscopic residual cancer remained; CC1-no nodule >2.5 mm in diameter remained; CC2-nodules 2.5 mm–2.5 cm in diameter remained; CC3-nodules >2.5 cm in diameter remained) [23]. In patients with CRC, only complete cytoreduction (i.e. CC0) is considered appropriate and included in this study. Perioperative complications in all patients were graded I to IV with increasing severity based on the Clavien-Dindo classification (Grade I: no treatment; Grade II: medications only; Grade III: surgical, endoscopic or radiological intervention; Grade IV: life-threatening complications requiring ICU admission) [7]. Major morbidity was defined as grade III or grade IV complications.

2.5. Chemotherapy

After complete CRS, but prior to intestinal anastomosis or repair of seromuscular tears, HIPEC was performed by installation of a heated chemoperfusate into the abdomen using the coliseum technique at approximately 42 °C. Oxaliplatin 350 mg/m^2 in 500mLs of 5% dextrose was given over 30 min or mitomycin C 12.5 mg/m^2 in 3 L of 1.5% dextrose peritoneal dialysis fluid if oxaliplatin in contraindicated.

2.6. Follow-up

All patients were followed up at monthly intervals for the first three months and six monthly intervals thereafter until the last time of contact or death. The follow-up review included clinical examination, measurement of tumour markers and assessment of CT scans with or without PET scans.

2.7. Statistical analysis

All statistical analyses were performed using IBM SPSS for Windows version 22. Comparison of normally distributed variables was performed using analysis of variance (one way-ANOVA) test. Categorical variables were analysed using the Chi-square test or Fisher' exact test where appropriate. Perioperative morbidity and mortality were the primary outcomes of this study. Hospital mortality was defined as any death that occurred during the same hospital admission for CRS. Median survival was calculated based on the date of death or last follow-up in the unit of months. Survival analysis was performed using the Kaplan-Meier curves and Log Rank test for comparison. Prognostic factors for survival were evaluated using the Cox proportional hazards regression model for the multivariate analysis. A significant difference was defined as P value < 0.05.

3. Results

3.1. Background characteristics

One hundred and sixty-eight patients with CRPC formed this study cohort. Between January 1996 and Oct 2015, 241 patients with CRPC were treated by our team. 52 patients were excluded due to synchronous liver metastases at the time of operation. 17 patients were excluded due to incomplete cytoreduction. 4 patients were excluded because no PIC was used. Table 1 provides a summary of the background characteristics of these patients. The mean age of our patients was 54.3 years old (standard deviation (SD) = 14.1). The mean PCI in this group was 9.5 (SD = 6.6). The mean unit of blood transfusion was 3.2 (SD = 3.4). 102 patients (60.7%) had retroperitoneal lymph node involvement at the time of operation. HIPEC was used in 161 patients (95.8%) whereas EPIC was only used in 55 patients (32.7%). 48 patients (28.6%) had HIPEC combined with EPIC, whereas 7 patients (4.2%) only had EPIC. There was a statistically difference in terms of diagnoses among five groups (p = 0.001). There was no statistical significance in terms of the use of HIPEC, oxaliplatin and EPIC among the six study cohorts (Table 1).