International Journal of Surgery 23 (2015) 181–185

Contents lists available at ScienceDirect

International Journal of Surgery

journal homepage: www.journal-surgery.net

Original research

Impacts of low peritoneal cancer index on the survival outcomes of patient with peritoneal carcinomatosis of colorectal origin

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HIGHLIGHTS

- We studied patients with CRPC and a very low PCI of 5 or less.
- The median survival of patients with low PCI in our study was 80.6 months.
- CRS and PIC has shown encouraging outcomes and offers hope for patients with CRPC.
- Early referral to specialist centre for evaluation is necessary.

ARTICLE INFO

Article history:
Received 30 May 2015
Received in revised form
8 August 2015
Accepted 15 August 2015
Available online 9 September 2015

Keywords:
Colorectal cancer
Peritoneal carcinomatosis
Peritoneal cancer index

ABSTRACT

Introduction: The combination of cytoreductive surgery (CRS) and perioperative chemotherapy (PIC) have been proposed as an innovative technique for peritoneal carcinomatosis and is currently considered as a standard treatment for colorectal peritoneal carcinomatosis (CRPC) in selected patients. Peritoneal cancer index (PCI) has been suggested to be the most important prognostic factors for the outcomes of patients with CRPC. In this paper, we have studied patients with CRPC and a very low PCI of 5 or less and their survival outcomes.

Methods: This is a retrospective study of prospectively collected data of 60 consecutive patients with CRPC and PCI $\leq$ 5, who underwent CRS and PIC by the same surgical team at St George hospital in Sydney, Australia between January 1996 and April 2015. Clinical outcomes of these patients were analysed.

Results: Hospital mortality was 0%. 14 patients (23.4%) had grade III/IV morbidity. The median follow-up was 22.2 months (range = 0.1–104.2). The median survival was 80.6 months (95% confidence interval (CI) = 35.1–126.1), with an overall 1-year, 3-year, and 5-year survival rate of 96.1%, 72.6% and 54.7% respectively. Among 60 patients, 31 patients experienced the recurrence of the disease (51.7%). The median disease-free survival was 10.8 months (95% CI = 7.2–14.4).

Conclusion: This innovative approach combining CRS and PIC has shown encouraging outcomes and offers hope for patients with CRPC. Our results suggest that CRS and PIC can be performed safely to provide significant survival benefits for patients with low volume of disease. Early referral to specialist centre for evaluation is warranted for better survival outcomes.

1. Introduction

In the past, colorectal peritoneal carcinomatosis (CRPC) was considered as a rapidly and universally fatal disease. Historically it was treated with systemic chemotherapy with or without palliative surgery, resulting in a median survival of six months [2]. It is characterised by the tumour deposits on the peritoneal surface either as a result of transcoleomic spread by the primary tumour or intraperitoneal seeding during surgical procedures. Disease progression will eventually lead to signs of bowel obstruction and

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http://dx.doi.org/10.1016/j.ijsu.2015.08.078
1743-9191/

incapacitating volumes of ascites [18].

Although systemic chemotherapy has evolved to achieve a median survival of 13 months ranging from 5 to 24 months, the long-term survival benefits are still limited with a 5-year survival rate of 6% ranging from 0 to 22% [1,3,4,6,10,12,15,16,19–22,27]. In the last two decades, the combination of cytoreductive surgery (CRS) and perioperative chemotherapy (PIC) have been proposed as an innovative technique for peritoneal carcinomatosis and is currently considered as a standard treatment for CRPC in selected patients [7,14,27,29]. CRS aims to remove all macroscopic peritoneal deposits and any bowel adhesions so that chemotherapeutic agents equally distributed intraperitoneally to eradicate any microscopic tumour, whereas PIC is used to achieve a high local concentration of cytotoxic drugs targeting residual microscopic disease [2]. PIC consists of hyperthermic intraperitoneal chemotherapy (HIPEC) and early postoperative intraperitoneal chemotherapy (EPIC).

The extent of CRPC, scored by peritoneal cancer index (PCI), as described by Jacquet and Sugarbaker [17], has been suggested to be one of the most important prognostic factors and most units have provided peritonectomy for patients with CRC and PCI less than 20. We introduced a limit of 15 in 2012. The most recent study done by Elias et al. (2014) has suggested that PCI $\leq$ 15 is associated with favourable survival outcomes [11]. Second look procedures are now advocated on the basis that patients with a lower PCI have a much better prognosis [8,9]. In this paper, we have studied patients with CRPC and a very low PCI of 5 or less and their survival outcomes.

2. Methods

2.1. Settings

This is a retrospective study of prospectively collected data of 60 consecutive patients with CRPC and PCI $\leq$ 5, who underwent CRS and PIC by the same surgical team at St George hospital in Sydney, Australia between January 1996 and April 2015. This was from a total of 225 patients treated by CRS and PIC for colorectal cancer during this time. 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 including surgical oncologists, medical oncologists, radiologists, cancer care nurses and research staff.

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-angiogram of the liver. Positron emission tomography (PET) was performed in all patients in addition to the stating laparoscopy to assess the PCI if the scans showed borderline results.

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. Cytoreductive surgery

An initial assessment of the volume and extent of disease was recorded using PCI. This assessment combines thickness 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 [25].

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 between 2.5 mm and 2.5 cm in diameter remained; CC3-nodules > 2.5 cm in diameter remained) [17]. Perioperative complications in all patients were graded I to IV with increasing severity based on the Clavien-Dindo classification of surgical complications (Grade I: no treatment; Grade II: medications only; Grade III: surgical, endoscopic or radiological intervention; Grade IV: life-threatening complication requiring ICU admission) [5].

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/m2 in 500mLs of 5% dextrose was given over 30 min or mitomycin C 12.5 mg/m2 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. A significant difference was defined as P value less than 0.05.

3. Results

3.1. Background characteristics

Between January 1996 and April 2015, 225 consecutive patients with CRCP were treated by our team. 60 of them had PCI less than or equal to 5. Table 1 summarises the background characteristics of these patients. The mean age of the patients is 58.7 years old (standard deviation (SD) = 13.1). The mean PCI in this group was 3.4 (SD = 1.3). The mean unit of blood transfusion was 1.9 units (SD = 2.1). All patients had a complete cytoreduction. 26 patients