

---

## Peer Review File

**Article information:** <http://dx.doi.org/10.21037/gs-20-893>

### Reviewer A

**This is a retrospective single-institution case-series of 4 patients who underwent cytoreductive surgery and HIPEC for breast cancer derived peritoneal metastases. The objective of this study was to provide evidence that this surgical management can be beneficial for such patients.**

1. **Comment 1:** First of all, I would like to point out that the overall English quality used in this manuscript is very poor and insufficient to consider publication in Gland Surgery. The manuscript was very difficult to read and interpret, especially the discussion. I would strongly advise the authors to have the paper reviewed by a linguist before considering submitting this paper again.

- Reply: we have made the meticulous language revisions as suggested (marked in red in the text).

**Here are some additional comments for the authors:**

2. **Comment 2 Introduction:**

- Page 2, lines 17-18: Please provide numbers and context for this sentence.
- **Reply:** We had added the numbers of the five-year survival and context for the sentence.
- **Changes in the text:** We have modified our text as advised (see page 2, line 17-18, page 11, line 21-22 and page 12 line 1).
- Page 2, lines 18-19: This sentence seems out of place, should be put before the prevalence of PC for breast cancer, with numbers and context, again.
- **Reply:** We had deleted the sentence and added the abbreviation PC in page 2, line 20 and the context in page 2, line 17-18.
- **Changes in the text:** We have modified our text as advised (see page 2, line

---

17-18 and page 2, line 20).

- Page 2, line 22: The authors should not use a sentence to describe an abbreviation...
- **Reply:** The sentence "'BC PC" means peritoneal metastases from breast cancer" had been deleted and the sentence "breast cancer peritoneal carcinomatosis (BC PC)" had been added in page 2, line 22.
- **Changes in the text:** We have modified our text as advised (see Page 2, line 22).
- Page 3, lines 1-4: These sentences are out of context and poorly written. Need to be rephrased entirely and need more development.
- **Reply:** These sentences were rephrased entirely.
- **Changes in the text:** We have modified our text as advised (see Page 2, line 21-22 and Page 3, line 1).
- Page 3, lines 5-6: The authors can't aim to "determine" the role of CRS + HIPEC with only 4 cases reported. Needs to be rephrased.
- **Reply:** The word "determine" had been replaced by "provide new ideas".
- **Changes in the text:** We have modified our text as advised (see Page 3, line 4).

### 3. Methods:

- Page 3, line 14: the presence of ascites is not included in the PCI. Did the authors include ascites in their PCI measurement for this study? If so, all PCI reported here are compromised...
- **Reply:** PCI score does not include ascites.
- **Changes in the text:** None.

### 4. Results:

- Case 4 had a PCI of 30, but only had hysterectomy and lymph nodes dissection as CRS. How?
  - **Reply:** Case 4 underwent total uterus, double, attachment, omentum, para-

---

aortic lymph nodes and pelvic lymph nodes as CRS (Table 2).

- **Changes in the text:** None.

- Figure 1 is irrelevant, as these figures have been widely used in a multitude of manuscripts before.

- **Reply:** We had deleted Figure 1.

- **Changes in the text:** We have modified our text as advised: **deleted** Fig. 1 A and Fig. 1 B and modified Fig. 2-5 to Fig. 1-4 (see Page 16, line 1,5,8, and 20).

- Figure 2 to 4: Is anything related to a specific patient? If so, it should be reported and identified this way, as this is just confusing right now.

- **Reply:** Figure 1-3 (Original Figure 2-4) are the preoperative CT, intraoperative and postoperative pathological photos of Case 1, respectively.

- **Changes in the text:** We have added “Case 1” modified our text as advised (see Page 7, line 16).

## 5. Discussion:

- Page 7, line 1: a case-series of 4 patients can't “demonstrate” a benefit. Needs to be rephrased...

- **Reply:** We had rephrased the conclusion.

- **Changes in the text:** We have modified our text as advised (see Page 7, line 4-6).

- The second paragraph of the discussion needs work, as it is confusing and hard to follow. We are left hanging and wondering what was the point of the paragraph to begin with.

- **Reply:** The second paragraph mainly explained the pathological types of breast cancer with peritoneal metastasis and analyzed the reasons.

- **Changes in the text:** None.

- Fourth paragraph: the authors cannot state that HIPEC prevents postoperative adhesions, because from a clinical point a view, this is simply false. There is no literature to support that.

- 
- **Reply:** We had deleted this sentence.
  - **Changes in the text:** We have modified our text as advised (see Page 8, line 12).

### **Reviewer B**

Authors present an interesting series of four patients treated with hyperthermic intraperitoneal chemotherapy for metastatic breast cancer. All patients failed multiple lines of previous therapies.

I have several questions for the authors;

1. All of the patients had massive malignant ascites. How many of them recurred?

- **Reply:** All 4 patients had no recurrence of ascites until the follow-up date.

- Changes in the text:** None.

2. The follow up for the patients is inadequate. Other than vital status what was the outcome.

- **Reply:** 4 patients had alleviated abdominal symptoms and no recurrence of ascites.

- Changes in the text:** None.

3. How are patients chosen for the procedure?

- Reply:** CRS+HIPEC were the standard treatment for PC and had formed a standard clinical path, including detailed inclusion and exclusion criteria.

Inclusion criteria: (1) have a clinical picture of BC PC and pathological confirmation; (2) have a Karnofsky performance status score  $\geq$  of 60; (3) have a normal peripheral blood white blood cell count  $\geq 3.5 \times 10^9/L$ , and a platelet count  $\geq 80 \times 10^9/L$ ; (4) have an acceptable liver function with bilirubin  $\leq 2 \times$  the upper limit of normal (ULN), and aspartic aminotransferase and alanine aminotransferase  $\leq 2 \times$  ULN; (5) have an acceptable renal function with serum creatinine  $\leq 1.2 \times$  ULN; and (6) have cardiovascular pulmonary and other major organ functions that could withstand a major operation. (Page 3, line 19-20

---

and Page 4, line 1-6)

exclusion criteria: 1) have bone, liver, lung, brain, or other distant metastases; 2) have serum bilirubin, aspartic aminotransferase and alanine aminotransferase levels  $> 2 \times \text{ULN}$ ; 3) have a serum creatinine level  $> 1.2 \times \text{ULN}$ ; 4) show significant mesenteric in a contracture imaging examination; and/or 5) could not withstand a major operation due to their general status or the functions of their major organs. (Page 4, line 7-12)

**-Changes in the text:** None.

4. The discussion talks about estrogen therapy, I suspect they mean anti-estrogen therapy

**-Reply:** I wrote anti-estrogen therapy as estrogen therapy because of my mistake.

**-Changes in the text:** "Estrogen therapy" has been replaced by "anti-estrogen therapy". (Page 2, line 21 and Page 9, line 8)

5. What was the survival after the hyperthermic intraperitoneal chemotherapy procedure?

**-Reply:** All 4 patients were survived until the follow-up date and overall survival from CRS+HIPEC were 31, 28, 15 and 49 months, respectively. (Page 6, line 20-21)

**-Changes in the text:** None.

### **Reviewer C**

1. There are multiple sentence structure and grammar mistakes in the main text, making it hard for readers to understand. Highly recommend engaging an editor that is well versed in medical terminology and the English Language to help with better phrasing of text.

**-Reply:** we have made the meticulous language revisions as suggested (marked in red in the text).

2. Presentation - Would be clearer if the 4 cases were presented as a 'Case Series', one

---

after another in the main text.

**-Reply:** The treatment processes of the 4 cases were similar so they were not presented as a 'Case Series'.

**-Changes in the text:** None.

3. Page 4, Line 14 (main text) - PCI is evaluated mainly based on lesion size scores in the respective abdominal regions, as illustrated in Fig. 1A. I am not sure that the severity of ascites contributes to the calculation of one's PCI. On that note, Figure 2A has a slight mistake. Tumours >5.0cm should have a score of LS-3.

**-Reply:** PCI score is based on tumor size and the severity of ascites is not. The highest PCI score is 39. Ascites in Figure 2A were not been used to evaluate PCI so there is no mistake.

**-Changes in the text:** None.

#### **Reviewer D**

Four case studies CRS/HIPEC for PC of breast Ca. There is so little existing data, this is useful.

**-Reply:** Thanks for your point.

**-Changes in the text:** None.