Reviewer’s report

Title: Cytoreductive Surgery and Hyperthermic Intra-operative Peritoneal Chemotherapy with Cisplatin for Gastric Peritoneal Carcinomatosis Monocentric phase-2 nonrandomized prospective clinical trial

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Reviewer: Mio Kitano

Reviewer's report:

The authors in this manuscript present the result of a single-institution phase II, non-randomized clinical study to evaluate long-term survival after CRS+HIPC with cisplatin in patients with gastric PC and to define selection criteria for this treatment modality. There is currently no sufficient data on survival benefit or patient selection criteria to recommend routine use of CRS+HIPC in patients with gastric PC. There were 32 patients who met selection criteria and they demonstrated median OS of 16 months in their entire study cohort and median OS of 24.7 months with 1-year OS rate of 90% in patients who had PCI scores <13 or no PC on small bowel combined with PC on <4 non-small bowel regions. The morbidity and mortality rates related to the procedure were 72% and 0%, respectively. They concluded that there is survival benefit in patients undergoing CRS+HIPC with cisplatin, provided a CCR-0 and R0 resection, in those patients with PCI scores below 13 and to those without PC on small bowel combined with PC on fewer than 4 non-small bowel regions.

This is a very well written manuscript and I commend the authors for addressing this controversial topic in a prospective manner.

In the method section, selection criteria is described in Table 1. Impossibility to obtain CCR-0 and R0 resection at the end of CRS are listed on the exclusion criteria. How were those criteria determined prior to intervention? Was this based on pre-operative imaging or diagnostic laparoscopy? What kind of imaging modality did the patients have prior to CRS (CT scan and/or MRI with peritoneal protocol)? Was diagnostic laparoscopy routinely employed in this study?

Among the exclusion criteria, clinical relevant ascites is listed. Please clarify the definition as most patients with PC will have some degree of ascites.

In the method section, you mention that there are 30 patients who received cisplatin-based systemic therapy in neoadjuvant setting and 22 in adjuvant setting. The numbers add up to 52 patients. Is this because 20 patients received both? Perhaps clarify by breaking them down into neoadjuvant, adjuvant, and peri-operative chemotherapy? How was the decision made who gets neoadjuvant vs adjuvant chemotherapy? Was there any survival benefit in patients who received perioperative chemotherapy?
XRT is allowed before or after to CRS+HIPC. Did any of the patients receive XRT? This is not mentioned in the result. If some patients received XRT, was there any impact on OS or DFS?

Some patients in this study presented with metachronous/recurrent disease. Did the initial stage at diagnosis have any impact on disease burden, OS, or DFS in those patients with recurrent disease? Did the patients with recurrent disease have lower disease burden as they should have been under surveillance and did patients with synchronous disease present with higher disease burden?

Figure 1 demonstrates OS after CRS+HIPC with cisplatin for PC. Both the KM curve and the Table demonstrating Number at risk divide the patient cohort into Group A and Group B. The groups, however, are described as Group 1 and Group 2 underneath the Number at risk table. Please clarify.

Figure 1 demonstrates OS after CRS+HIPC with cisplatin for PC. On the Table demonstrating the number at risk, what time interval does each column represent?

The authors concluded that there is survival benefit in patients undergoing CRS+HIPC with cisplatin, provided a CCR-0 and R0 resection, in those patients with PCI scores below 13 and to those without PC on small bowel combined with PC on fewer than 4 non-small bowel regions. On the Figure 1 legend, definition of Group1 (A) and Group 2 (B) is confusing. Groups 1 (A) is the "favorable" group as mentioned in author's conclusion. Why do the numbers overlap? Shouldn't Group 2 (B) have PCI >14 or the presence of PC on the small bowel plus >5 non-small bowel regions?

The authors mention in discussion that CCR-0 and R0 resection are important determinants for this (their favorable) outcome. Patients who were deemed impossible to undergo CCR-0 and R0 resection were excluded from the study. This study included highly selected patients who could undergo CCR-0 and R0 resection, therefore, this is not a fair statement as they did not compare CCR-1 and R0 vs non-CCR-1 and R1-2 patients on patient outcomes.

The authors mention in discussion, "Other factors with a positive effect on survival are the absence of post-operative mortality, appropriate selection of patients, and high rate of systemic chemotherapy in neo-adjuvant and adjuvant settings". How did the authors arrive to this statement and please clarify, as according to Table 2, there was no statistical significance in use of neoadjuvant or adjuvant chemotherapy on OS. Additionally, is it a fair statement of say absence of post-operative mortality has positive effect on survival? Especially, since there was no mortality in this study?

In the background, there should be an appropriate reference(s) after the sentence on line 51 of page 4, after "...offering patients improved survival".
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Unable to assess

Are the conclusions drawn adequately supported by the data shown?
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Yes

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