

Peer Review File

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Reviewer Comments

Comment 1: There was similar report (Clin Nutr. 2020 Feb 22:S0261-5614(20)30080-7) in the PubMed. What is the novel idea in the paper? Please elaborate in the introduction.

Reply 1: Thank you for teaching us an important paper by Dolly et al. However, while they investigated the changes in BMD before and after systemic chemotherapy in patients with metastatic CRC, our paper focused on the impact of low BMD on survival outcomes of patients with resected CRLM and might be essentially different from their paper. In any case, that is a valuable paper for us, and we have cited that in the manuscript.

Changes in the text: The paper by Dolly et al. was added as a new reference (No. 14) and cited in the introduction (Page 5, Line 9) and discussion (Page 13, Line 8) sections.

Comment 2: In the introduction, please enrich the progress of the treatment for CRC.

Reply 9: According to your valuable comments, we have added to the introduction about progress in treatment for CRC, with a new reference (No. 3).

Changes in the text: The following sentences were inserted in the introduction: “Over the past several decades considerable progress has been made in the management of metastatic CRC leading to a significant improvement in 5- year survival. Some of this success has been rightly attributed to aggressive surgical management and advances in other adjunct treatments (3).” (Page 4, Line 5-9). Additionally, in considering the context, we changed the following sentence, “Even patients with initially unresectable CRLM can sometimes be cured after liver resection as a result of recent advances in operative methods, systemic chemotherapy, and targeted therapy (4).” to “Even patients with initially unresectable CRLM can sometimes be cured with multidisciplinary treatment, including staged liver resection, systemic chemotherapy, and targeted therapy (6).” (Page 4, Line 12-14).

Comment 3: Are there any metastases in CRC patients? Please supplement in the introduction.

Reply 3: (We hope we haven't misunderstood the question.) All our patients had liver metastases and 64 of them had extrahepatic metastases at the time of liver resection. If you point out that the general frequency of distant metastases in CRC patients should be described in the introduction, we have added about it.

Changes in the text: We changed the following sentence in the introduction, with a new reference (No. 2). ” Approximately half of CRC patients develop liver metastases at some point in their course of disease.” to “About 25% of CRC patients present with distant metastases at diagnosis, and approximately half of patients will develop liver metastases at some point in their course of disease (2).” (Page 4, Line 3-5).

Comment 4: What is the meaning of “CLRM patients” in the introduction?

Reply 9: To avoid redundancy, we described "patients with colorectal liver metastases" as "CRLM patients" throughout the paper. As you pointed out, there was a part where we inadvertently wrote "CRLM" as "CLRM" in the introduction, and we have corrected it.

Changes in the text: "CLRM" was changed to "CRLM" (Page 4, Line 16; Page 5, Line 3; Page 6, Line 2).

Comment 5: Whether the enrolled patients underwent colorectal resection? What are the inclusion and exclusion criteria for enrolled patients?

Reply 5: Patients who did not have a primary tumor resection at the time of observation were excluded from the study, as described in Page 6, Line 13. The inclusion and exclusion criteria for enrolled patients were shown in Page 6, Line 7-14.

Changes in the text: no changes are made.

Comment 6: How to measure the CEA level? Please supplement in the methods.

Reply 9: The CEA serum level was determined preoperatively using a commercially available immunoassay kit.

Changes in the text: The following sentence was inserted in the methods: "The serum tumor marker levels were measured within one month before liver resection using the chemiluminescent enzyme immunoassay kit (Fujirebio, Tokyo, Japan) for carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9" (Page 6, Line 16- Page 7, Line 1).

Comment 7: What are the diagnostic criteria for CRLM?

Reply 7: All enrolled patients were diagnosed having CRLM in microscopic examination of the resected liver specimens.

Changes in the text: We have changed the following sentence, "310 consecutive patients with CRLM who underwent..." to "310 consecutive patients with histopathologically proven CRLM who underwent..." (Page 6, Line 8).

Comment 8: Why the BMD can be used to estimate CRLM patient? Please supplement in the discussion.

Reply 8: If your question means "Why the BMD can be used to estimate CRLM patient prognosis?", then that is exactly what we have considered in the discussion. We have discussed the following points: (1) BMD estimation using routine CT images is a simple and reliable method that requires no additional cost (Discussion, Para 1). (2) Low BMD may reflect a high tumor burden and/or may be an effect of chemotherapy before liver resection (Discussion, Para 2-3). (3) Low BMD may be associated with future physical activity decline which make long-term anticancer therapy difficult, or with non-cancer mortality (Discussion, Para 4).

Changes in the text: no changes are made.

Comment 9: Please provide representative images of CT measured BMD in the paper.

Reply 9: According to your suggestion, we added representative CT images as new Figure 1.

Changes in the text: The new Figure 1 was mentioned in the main text (Page 8, Line 7) and figure legends (Page 23, Line 2-3). Along with this, the original Figures 1 and 2 were changed to Figures 2 and 3, respectively.