

Peer Review File

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Reviewer A

I think the work is well planned and written correctly with a good level of English. The reviewer congratulates the authors for their work and understands the difficulty of the study, because it is not easy to analyze patients with a disease as advanced as the advanced stages of colorectal cancer. However, there are several details that must be corrected before the article can be considered as publishable and they are listed below:

Comment 1: – Line 41: the abbreviation “MBD” is not specified anywhere

Reply 1: Thank you for your comment. We added “Metastatic bone disease” as a specification of the abbreviation “MBD”.

Changes in the text: Please see amendment page 3 line 44-45.

Comment 2: – Line 44: "article / case". The reviewer understands the work presented as an article, better delete the word case.

Reply 2: We removed the word case as suggested by the reviewer.

Changes in the text: Please see page 3, line 47.

Comment 3: – Line 80: "(figure 1)". Two figures are presented under the nomenclature figure 1. It should be specified that the author means "figure 1A"

Reply 3: Thank you for your remark. We specified the nomenclature “figure 1” as “figure 1A”.

Changes in the text: See page 5, line 91.

Comment 4: – Line 81-82: "The neurological symptoms were classified according to the Frankel scoring system (2)". This sentence belongs to the section on material and methods.

Reply 4: We move the sentence "The neurological symptoms were classified according to the Frankel scoring system (2)" to the section on material and methods as advised. We also added the following short sentence to introduce this classification “Indications for surgery were pain, major neurological deficit or inability to weight bare”.

Changes in the text: See page 4, line 67-69.

Comment 5: – Line 88-89: The reviewer considers it unnecessary to present the photo of a particular case, when what is intended to expose is a series of patients. This image does not provide useful information in the interpretation of the article. In the opinion of the reviewer, the photo should be removed.

Reply 5: We removed the photo as recommended by the reviewer.

Changes in the text: See page 6, line 100.

Comment 6: – Line 96-98: "The third patient presented with skeletal metastasis of unknown origin at the time of surgery and was not given any cytostatic treatment within the follow-up period". This

phrase is perhaps a rather serious error when interpreting the study. The author, when setting up the study, specifies that all patients have metastases of colorectal origin; How then can he say that the third patient has a bone mass of unknown origin?

Reply 6: Thank you for this remark. We added some information to explain this further.

Changes in the text: See page 6, line 107-110.

Comment 7: – Line 146-148: "solitary bone metastasis, even with the presence of visceral metastasis, was a good prognostic factor for survival". This conclusion is misleading. The author is requested to correct it and improve the concept to be communicated.

Reply 7: We changed the sentence to make the concept we tried to communicate more clear.

Changes in the text: See page 9, line 165-167.

Comment 8: -Table 1, Table 2, Table 3: The reviewer finds missing in all the tables the percentages that generally accompany the presentation of the data. The journal publication standards should be reviewed and this aspect improved.

Reply 8: Thank you for your input. We adjusted the table according to the journal standard and added percentage as requested.

Changes in the text: See Table 1, Table 2 and Table 3.

Reviewer B

Comment 10: Considering the poor prognosis of patients with MDB for CRC and the high rates of operation, could you define which patient do really benefit of surgery and which not (e.g.. only radio-chemotherapy, palliative pain therapy...)

Reply 10: Thank you for your input which helps us improve our article. We added some information regarding which patients that benefit from surgery as advised.

Changes in the text: See page 8, line 159-161.

Comment 11: Missing data about the true incidence of MDB for CRC in the literature

Reply 11: We now provide more detailed description of the incidence of MBD in CRC.

Changes in the text: See page 35, line 38-42.

Reviewer C

This is an interesting article about an important topic, which is not very well described in the literature. The authors present their experience clearly.

Comment 12: It would help if the authors can mention how long after the surgery for the colorectal cancer did the bony metastases occur.

Reply 12: Thank you for your input that help us improve our article. We added some date reading the onset of skeletal event after CRC surgery as requested.

Changes in the text: Please see page 5, line 78-84.

Comment 13: Also it may be a good idea if the authors can find out whether any features of the primary malignancy might be related to bony metastases (e.g nodal status, diameter of tumor, resection margin status, etc.)

Reply 13: Thank you for your comment. We tried to specify the features of the tumor but found it hard to find in our charts. Documentation was missing for most of the patients regarding nodal status. We did not do any analysis of the primary tumors, since it was not within the scope of this study, and there are no data that support the hypothesis that primary tumor margins are important to the development of bone metastasis, and such an explorative study would not be appropriate in a relatively limited cohort such as the one we elaborate on.

Changes in the text: No changes.

Comment 14: The authors could also mention a literature review on the topic. Although rare, there are isolated case reports of short to long term survival after resection of bony metastases. (Cassar et al. DOI: 10.1007/s00384-017-2780-1 Oligometastatic colorectal cancer: is single-site bony colorectal metastasis a treatable condition?)

Reply 14: We've now added a sentence about this topic as advised.

Changes in the text: See page 8, line 162-164.