

Dear Prof. Ma and Reviewers:

Thank you for your letter and for the reviewers' comments concerning our manuscript entitled "Advances in Liver Transplantation for Unresectable Colon Cancer Liver Metastasis" (Manuscript NO.: 69522, Minireviews). Those comments are all valuable and very helpful for revising and improving our paper. We have studied comments carefully and have made correction which we hope to meet with your standard. The corrections in the paper and the responds to the reviewers' comments are as following. If there is any requirement and question, please tell us.

Thank you and best regards.

Yours sincerely,  
Hui Hou. M.D

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Reviewer #1:

Thank you for your comments

Reviewer #2

1- The new colorectal cancer cases and related death in 2020 has been released recently (PMID: 33538338, PMID: 34243011), please use the new statistics.

Answer: We had replaced the old citation with the former one in the first paragraph.

2- Some of the abbreviations in the tables should be clarified.

Answer: Thank you for suggestion, we have added these missing informations.

PFS, Progression Free Survival; MRI, Magnetic Resonance Imaging; Randomized clinical trial (RCT); FOLFOX, Fluorouracil and oxaliplatin; mFOLFOX-6, modified 5-fluorouracil/folinic acid and oxaliplatin); FOLFIRI, Fluorouracil, folinic acid, and irinotecan; TACE, transcatheter arterial chemoembolization; Y-90, Yttrium; RFA, Radiofrequency ablation; FLIRI, 5-fluorouracil, leucovorin and irinotecan (**Modified on page 1, line 23-34, Table 2 and Table 3**)

3- The correspondence author's Email address seems not from the correspondence author, please confirm it.

Answer: Sorry, we have corrected it.

hui0402@hotmail.com (**Modified on page 1, line 17**)

4- There are some spelling and grammatical errors, the author should check it carefully.

Answer: We have revisited the language and gotten the polishing certification. The

revisited parts are as following:

#### **Abstract section:**

- 1, line 2 **gives** was replaced with **provides**
- 2, line 3 **Approximately twenty percent of patients have resectable CRLM** was deleted.
- 3, line 5 **In addition to** was replaced with **In addition to the**
- 4, line 8 **Curable** was replaced with **curative**
- 5, line 10 **strategy** was replaced with **strategies**
- 6, line 11 **have not been well defined** was replaced with **are lacking**
- 7, line 12 **was performed to discuss the views** was replaced with **discusses views on**
- 8, line 13 **advance** was replaced with **advances**
- 9, line 16 **A literature review was executed in published articles and registered clinical trials in the Pubmed, Goolge Scholar, Clinicaltrials.gov relevant to LT for CRLM** was replaced with **A literature review of published articles and registered clinical trials in PubMed, Google Scholar, and Clinicaltrials.gov was performed to identify studies related to LT for CRLM**
- 10, line 20 **Patients with good performance, tumor biology behavior is good and chemosensitivity are mainly candidate selection criterion** was replaced with **The main candidate selection criteria are good patient performance, good tumor biological behavior and chemosensitivity**
- 11, line 21 **Chemotherapy should be necessarily administrated before transplant, but not commonly post-transplant for preventive purpose** was replaced with **Chemotherapy should be administered before transplantation but is not commonly administered posttransplantation for preventive purposes**
- 12, line 26 **efficient to meet** replaced with **efficient means to resolve**
- 13, line 27 **proved** was replaced with **proven**

#### **Introduction section**

- 1, Paragraph 1, line 1, **2018** was replace with **2020**, actually the amount of new cases and predicted death were coincidence in both two paper.
- 2, Paragraph 2, line 6 **remained stagnant** was replaced with **received little attention**

#### **The selection criteria for LT in candidates with unresectable CRLM**

- 1, Paragraph 1, line 1 **limited study experience** was replaced with **the limited number of study**
- 2, Paragraph 1, line 8 **R0 liver resection and organ deficiency** was replaced with **that achieved by R0 liver resection and the deficiency of organs for transplantation**
- 3, Paragraph 1, line 12 **negative** was replaced with **negativity**

4, Paragraph 2, line 13, with negative lymph nodes and negative p53 or K-Ras mutations showed a significantly longer OS was replaced with **than patients with positive lymph nodes and p53 or K-RAS mutations**

5, Paragraph 3 line 9, liver transplantation in which patients was replaced with **LT, suggesting that**

6, Paragraph 5, line 3, on response evaluation criteria in solid tumors beyond 8 weeks or longer was replaced with **based on Response Evaluation Criteria in Solid Tumors at 8 weeks or beyond**

7, Paragraph 6, line 3, With the increasing number of trial outcomes in the future was replaced with **With the increasing number of trials whose outcomes are awaited**

### **Peritransplantation chemotherapy for unresectable CRLM section**

1, Paragraph 4, line 5 Adjuvant chemotherapy combined or not with immune checkpoint inhibitors was replaced with **Adjuvant chemotherapy combined with immune checkpoint inhibitors or without combination**

### **Posttransplantation immunosuppression and oncological safety**

1, Paragraph 2, line 17, but it is highly recommended to switch to mTOR inhibition from CNIs when there is a risk of malignancy was replaced with **it is highly recommended to switch from CNIs to mTOR inhibitors**

2, Paragraph 5, line 3 keeps the balance between antiproliferative and rejection effects at relatively lower CNI levels was replaced with **The use of relatively low CNI levels in the early posttransplantation period keeps keeps the balance between antiproliferative and rejection effects**

### **Advances in LT surgery for CRLM section**

1, Paragraph 2 line 6 immunosuppressive regimens posttransplantation do not increase

CRLM recurrence in comparison to CRLM without these regimens was replaced with Immunosuppressive regimens posttransplantation do not increase CRLM recurrence in comparison with no immunosuppressive regimens

2, Paragraph 5, line 2 Eleven patients with unresectable CRLM had undergone RAPID surgery using deceased donor (DD) grafts and living donor (LD) grafts by the end of 2019, specifically eight patients with LD-RAPID (five in Germany, two in Italy, and one in Belgium) was replaced with Eleven patients with unresectable CRLM, specifically eight patients with LD-RAPID (five in Germany, two in Italy, and one in Belgium) had undergone RAPID surgery using deceased donor (DD) grafts and living donor (LD) grafts by the end of 2019

## **Conclusion section**

Paragraph 1, line 1, the 2- and 5-year OS rate was 10% was replaced with the 2- and 5-year OS have been found to be 10%

Paragraph 2, line 1, The resolution for this was replaced with Resolution of these challenges

Paragraph 5, line 2 How to define suitable second surgical occasions between ensuring was replaced with defining suitable second surgical indications that both ensure