

We feel great thanks for your professional review work on our article. As you are concerned, there are several problems that need to be addressed. According to your nice suggestions, we have made extensive corrections to our previous draft, the detailed corrections are listed below.

**Reply to Reviewer #2:**

Specific Comments to Authors: Thank you very much for asking me to review this manuscript by Shiyang Li et al. This is a retrospective study to explore de novo CR. Therefore, there was no a complete study about de novo CRC, the authors in this study constructed a comprehensive system for diagnosis and treatment of de novo CRC. The result of the study is of interest and may provide strategy for differentiating de novo CRCs during colonoscopy examination. Overall, this study was well conducted with good methodology. It emphasizes the high metastatic potential of de novo CRCs. Furthermore, minor comment that I would to proposed:**1. Title:** I suggest to clarify that the article in the title is a retrospective study.

**#Answer: Thank you for your very kind advice. We have changed the title into Endoscopic and pathological characteristics of de novo colorectal cancer: a retrospective cohort study.**

2. Abstract: Address all of the important component from the study.

Thank you very much.

3. Key words: could cover this study.

Thank you very much.

4. Introduction: Describe the overall basic knowledge for this study. Moreover, the aim of the study is clear.

Thank you very much.

5. Method: The present study is methodologically well conducted.

Thank you very much.

6. Results: The result of this study is of interest.

Thank you very much.

7. Discussion: The manuscript clearly interprets the finding adequately and appropriately. In addition, the manuscript highlights the key points clearly. The previous significant paper involved were included in the discussion, I suggest to add the significance of the study and what further research is required.

**#Answer: Thank you for your very kind advice. After consideration, we decided to insert the following in the discussion part.**

**This study have several promising implications during clinical practice. Due to the highly invasive and metastatic ability of de novo CRC, Endoscopic Mucosal Resection (EMR) or Endoscopic Submucosal Dissection (ESD) could not be performed without exact observation when we find small protruded or depressed lesions. Observing the lesions with magnified endoscopy and chromoendoscopy is necessary to confirm the diagnosis. If we suspect the lesions may be de novo CRCs, it is crucial**

evaluating invasion depth by magnified endoscopy and chromoendoscopy , or by Computed Tomography (CT) imaging and EUS when necessary. Then, the treatment regimens should be chosen cautiously. In the future , we will further study the molecular biological difference between de novo CRC and CIA CRC to find out the molecular mechanism of invasion and metastasis of de novo CRCs.

8. Tables and figures: I congratulate the authors for the captions to the tables and figures very explicative and complete. However, All Figures regarding endoscopic findings require a scale.

**#Answer: Thank you for your important advice. We have inserted a scale into every histopathological picture, and also identified endoscopic images with different light sources. I am very sorry that there is no scale for the endoscopic images obtained during the intensive magnification examination, because the magnification could not be fixed.**

9. References: The manuscript reviewed previous related literature.  
Thank you very much.