

Dr. Ke Chen
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Dear Dr Chen,

We would like to thank the reviewers for their useful comments. We have revised our manuscript accordingly, as outlined below.

Reviewer 1 (Reviewer's code: 02575643)

- Comments; 6

First of all , thank you for your excellent review and advice.

1.Interesting paper. The negative aspect is that it is a retrospective analysis, with all the possibilities of biases, including a clear preference from the Authors to demonstrate that laparoscopic surgery is superior to conventional surgery for T4 colorectal cancers. In the discussion the Authors should underline clearly the possibility of biases from a retrospective analysis.

- Yes, as a retrospective study, it is inevitable that the selection bias exists. This study did for pT4 colorectal cancer, we also mentioned in the article, the decision to proceed with laparoscopy or open surgery was made for all subjects on a patient-by-patient basis following multidisciplinary discussions and meetings as preoperative CT and MRI were used to determine the preoperative clinical stage. However, for surgeons, always selecting open surgery for patients with T4b, large tumors, older, and poor cardiopulmonary function. And this is the reason that there are differences in the T stage between the LAP group and the OPEN group($p=0.021$). Finally, in the conclusion section of the article, we also discuss the limitations of this study as a retrospective study.

2.The Authors excluded from their analysis low rectal cancers. They should explain why and which were the results in this subgroup of patients.

- Because of the differences in preoperative and intraoperative therapeutic strategies for low rectal cancer, the study will be cued to minimize the impact on prognostic analysis.

3.I am concerned with the high number of patients with neagtive nodes. All together there were more than 30% of the patients with negative nodes. This is quite different from general statistica on colorectal cancer, when T4 cancers have a prevalence of lymph node involvement superior to 60%.

This situation of high percentage of patients with negative nodes is casual or does it derive from a selection of the patients or to inadequate lymph node dissection and removal? This point should vbe addressed in the discussion.

- In our study, the negative lymph node rate was slightly lower than in some studies, at 34.5%. This is associated with the exclusion of distant metastases and palliative resections cases. In and de'Angelis N 's study, negative lymph node rates were similar to our study.

【】 de'Angelis N. International journal of colorectal disease 2016; 31(11): 1785-1797

【】 Shukla PJ. Diseases of the colon and rectum 2015; 58(1): 25-31

4.The Introduction is too long and it should be shortened. They report the series of patients with T4 colorectal cancer who had surgery. Probably it could be interesting to report several series in which open and laparoscopic surgery were used in T4 patients.

- We have shorten our introduction. From Table 7, we make a complete review that studies about laparoscopic surgery for pT4 colorectal cancer.

5.Finally, the approach and technique they used in open and laparoscopic should be reported in detail (with figures) to have some possibilities to compare their data with other centres.

-In our article, we said that the approach and technique we used in open and laparoscopic surgery just according to the Japanese Society for Cancer of the Colon and Rectum (JSCCR) Guidelines [9], which have the following requirements: D3 lymph node dissection (Figure 1).And in our discussion and table 7, we compared our data with other centres.

6.One of the major problems in extrapolating data from Asian countries to western countries is the size of the patients. It is very easy to perform, even very difficult surgery, in thiny asiatic patients. On the other hand the same operation can be very difficult in an obese or very athletic western man.

- In the discussion section, we explain differences in conversion rates between Asian countries and western countries as follows: 1. Laparoscopic technology and experience may differ between Asian and Western countries; 2. the conversion standard was different; 3. there is a lack of preoperative imaging assessments to select appropriate laparoscopic surgery cases in Western countries; 4. European populations had a higher BMI.

Reviewer 2 (Reviewer's code: 02570566)

- Comments; 1

1. The title of this manuscript is that the short-term and long-term outcomes following laparoscopic versus open surgery for pathological T4 colorectal cancer: 10 years of experience in a single center. In this study, the author retrospectively analyzed the short- and long-term outcomes of proven pathological T4 colorectal cancer patients from 2006 to 2015 in Guangdong General Hospital. The authors demonstrate that the laparoscopy is safely used in the treatment of Pt4 colorectal cancer while offering advantages of minimal invasiveness and faster recovery. Experiments are well designed and the manuscript is well written.

-Thank you for your excellent review and advice.

Reviewer 3 (Reviewer's code: 02533764)

First of all , thank you for your excellent review and advice like following: The manuscript submitted by Yang et al., entitled “Short-term and long-term outcomes following laparoscopic versus open surgery for pathological T4 colorectal cancer: 10 years of experience in a single center” described feasibility of laparoscopic surgery for T4 colorectal cancer. It is one of the important issues and of interest. Major concerns exist to address.

- Comments; 5

1. Figure 1 is not authors' own figure.

-The figure referenced from JSCCR Guidelines .In our article, the section of “Surgical procedure”, we mentioned that all cases entailed surgical resection according to the Japanese Society for Cancer of the Colon and Rectum (JSCCR) Guidelines [9], which have the following requirements: D3 lymph node dissection (Figure 1). And the figure legend of Figure1 is revised as Flowchart for selection of the extent of lymph node dissection (from reference 9)

2. Table 2 showed that resection length between laparoscopic and open group is statistically different. The reason why it has difference should be described.

- There was a difference between the two groups in resection length, the main reason may be related to the wider scope of T4 tumor involvement in the open group, more T4b cases, more cases of combined organ resection in OPEN group. In Park's study, they also showed the similar result.

[] Park JS, Huh JW, Park YA, Cho YB, Yun SH, Kim HC, Lee WY, Chun HK. Clinically suspected T4 colorectal cancer may be resected using a laparoscopic approach. BMC cancer 2016; 16: 714

3. Table 3 presented that pT4 stage between laparoscopic and open group is statistically different. It means that background of patients was different in both groups. Therefore, two groups could not be compared. Actually, Figure 3 and 4 indicated that laparoscopic group had a tendency toward better survival than open group.

- The negative aspect of our study is that it is a retrospective analysis, with all the possibilities of biases, including a clear preference from the Authors to demonstrate that laparoscopic surgery is superior to conventional surgery for T4 colorectal cancers. Surgeons always selecting open surgery for patients with T4b, large tumors, older, and poor cardiopulmonary function. And this is the reason that there are differences in the T stage between the LAP group and the OPEN group(p=0.021). Laparoscopy showed a good prognosis tendency, maybe because there are less T4b cases and combined organ resection in LAP group. This result is similar to Park, Kang and de'Angelis N's studies.

[Park JS, Huh JW, Park YA, Cho YB, Yun SH, Kim HC, Lee WY, Chun HK. Clinically suspected T4 colorectal cancer may be resected using a laparoscopic approach. BMC cancer 2016; 16: 714

[Kang J, Baik SH, Lee KY, Sohn SK. Outcomes of laparoscopic surgery in pathologic T4 colon cancers compared to those of open surgery. International journal of colorectal disease 2017; 32(4): 531-538

[de'Angelis N, Landi F, Vitali GC, Memeo R, Martinez-Perez A, Solis A, Assalino M, Vallribera F, Mercoli HA, Marescaux J, Mutter D, Ris F, Espin E, Brunetti F. Multicentre propensity score-matched analysis of laparoscopic versus open surgery for T4 rectal cancer. Surgical endoscopy 2017; 31(8): 3106-3121

4. Table 3 included HER2 status. This study is for colorectal cancer. Why was HER2 examined?

- Currently, the significance of HER2 in colorectal cancer remains controversial. Our center has tested this indicator since 2003 and now we are currently exploring its significance, especially in T4 colorectal cancer.

5. Table 5 and 6 demonstrated that CA19-9 is better marker for survival than CEA. In general, CEA is much better marker for colorectal cancer than CA19-9. Does Hazard Ratio of CEA 0.6 in Table 5 mean better survival? Authors should discuss with statistician.

- Yes, many studies support CEA as a better prognosis to predict the prognosis of colorectal cancer. Similarly, CA19-9 also predicts prognosis. Our study is aimed at pT4 colorectal cancer which is different from the type of

early colorectal cancer. All the retrospectively collected data from Table 7 have not been analyzed CA19-9 as a prognostic indicator. Our study found that CA19 -9 might be a better predictors in T4 colorectal cancer which may lead a clinical help, but this study is only a small and retrospective study, all the results are only a hint.

Other revision

- We initially submitted this article after English language editing by AJE company. The revised article was submitted after a second round of English language editing.

We confirm that this manuscript has not been published elsewhere and is not under consideration by another journal. All authors have approved the manuscript and agree with submission to *World Journal of Gastroenterology*. The authors have no conflicts of interest to declare.

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We look forward to hearing from you at your earliest convenience.