

ANSWERING REVIEWERS

Dear Editor,

We appreciate the opportunity to revise our manuscript entitled “Endoscopic Submucosal Dissection of Gastric Tumors: A Systematic Review and Meta-analysis” for consideration for publication in the *World Journal of Gastrointestinal Endoscopy*. We have responded to the editor’s comments as well as reviewer’s suggestions, and updated our manuscript to address important issues raised in the review. We believe this has significantly improved our manuscript.

The manuscript has not been previously published in whole or in part, nor is it under consideration for publication elsewhere.

We look forward to hearing from you.

Sincerely,

Gen-shu Wang, MD,PHD

Below are our responses to reviewers’ comments:

Comment 1: The authors have presented a meta analysis of studies that compare minimally invasive and conventional living liver donation. The studies included are a mixed bag and include some laparoscopic, some true laparoscopic assisted and some partly laparoscopic with a subsequent midline incision. None of these studies were randomised but had retrospective control groups of open LRLD. The authors do however acknowledge that this weakens their data. the manuscript is well written with a few grammatical & spelling errors. It is encouraging to see that the authors have not exaggerated their conclusions and overall I believe that the manuscript is worthy of publication.

Response: Thank you for your consideration of our article and giving us so much precious comments. We cherish these comments very much and have modified the grammatical and spelling errors. Thank you very much!

Comment 2: Firstly, I think that a surgical approach of upper midline incision length >15 cm in a left-side living donor hepatectomy is unlikely at present. Therefore, all of the left-side living donor hepatectomy is classified as minimally invasive procedures, and the analysis of left-side living donor hepatectomy is meaningless. I think that the analysis of right-side living donor hepatectomy is meaningless. Only the analysis of right-side living donor hepatectomy is sufficient to demonstrate an efficacy of minimally invasive living donor hepatectomy. In addition, it is difficult to understand its efficacy because of too long manuscript. Secondly, it is necessary to distinguish between early (1990 's(or -2010's)) and late (2000 's-(or 2010's-)) periods. The progress of surgical procedures is different between early (1990 's(or -2010's)) and late (2000 's-(or 2010's-)) periods. I think that it is not suitable to analyze the study including both early (1990 's(or -2010's)) and late (2000 's-(or 2010's-)) periods.

Response: The table below showed the characteristics of the selected articles (table 1). Of all the thirteen literatures, four studies analyzed left-side living donor liver resection. The surgical approach of upper midline invasive approach was applied to left-side living donor hepatectomy after 2008. And with the development of surgical techniques, the surgical incision became increasingly short. But in some areas, such as China, the upper midline incision length still usually exceeded 15 centimeter. The studies concerned living donor left hepatectomy were comparing laparoscopic or laparoscopy-assisted approaches with open approaches. The incision length of laparoscopic-related approaches was shorter than open ways. In some literatures, it defined incision length <15cm as minimally invasive approach. More studies only comparing different approaches for right-side living donor hepatectomy are around the corner.

Since the first report of minimally invasive living donor liver transplantation, the surgical techniques were improved and perfected continuously. And a variety of minimally invasive approaches were applied to graft harvest for

living donor liver transplantation. We agree that it is necessary to distinguish between early and late periods. Most of the 1593 cases included in selected studies were accomplished after 2010. We once thought about removing articles before 2010, but we chose to keep these literatures in the end. Because all the studies balanced conditions between MILDH group and CLDH group, including the surgeon groups and the decade of operations. There were few cases regarding minimally invasive living donor hepatectomy before 2010 because of the difficulty of this technique, therefore few centers could perform MILDH. As time went on, more and more laparoscopic liver resection were performed. The techniques of the surgeon groups improved constantly and effective surgical instruments applied to the operation leading to more diverse ways for living donor liver resection. After 2010, minimally invasive living donor hepatectomy was performed more frequently, this made us interested in the study. We want to obtain the result which comparing the advantages and disadvantages of these two kinds of operative approaches, so we think the operative year is not the most important aspect for the comparison between the two kinds of operation methods. What we do is to collect available literatures and analyze them comprehensively, this requires a comprehensive literature search and elaborate selection. In the final included studies, each article was performed in a single center. Then the improvement of surgeon groups' technique would be embodied in the two groups at the same time, not only MILDH group. It is inevitable that getting the difference of operative results in different years. It is inconvenient to group analysis according to the operative years due to the less number of related literature. If there is more data in the future, it is feasible to analyze minimally invasive approaches performed in the late period only.

Table characteristics of included studies

Study no.	patient no.		Left/right	Year	TMI*	TCI*
	MILDH*	CLDH*	*			
Baker et al. [2009]	33	33	right	2004.04-2008.05	LA*	Midline epigastric
Choi,H et al. [2012]	60	90	right	2008.10-2011.05	LA	Right subcostal
Choi,Y et al. [2014]	25	484	right	2007.04-2012.12	HAL* or LA	Mercedes-Benz or L-

						shaped
Kim,S et al. [2009]	23	23	right	2005.01-2008.05	Upper midline	J-shaped
Kim,K et al. [2011]	11	11	left	2008.05-2009.10	L*	J-shaped or midline
Makk et al.2014	26	24	right	2011.12-2013.04	LA	Right subcostal with midline extension
Marubashi et al.2013	31	79	left	2009.04-2012.03	LA	Mercedes
Nagi et al.2012	28	30	right	2000-2011	Hal or upper midline	Mercedes
Samstein et al.2015	22	20	left	2003.05-2014.05	L	Midline
Soubrane et al.2006	16	14	left	1998-2005	L	Subcostal
Suh et al.2015	161	268	Un*	2010.04-2013.02	LA or Upper midline	L-shaped
Thenappan et al.2011	15	15	Un	2005-2009	LA or Minimally-access	Midline epigastric with subcostal
Zhang et al.2013	25	25	right	2011.07-2013.03	LA	Right subcostal

MILDH = Minimally invasive living donor hepatectomy; CLDH = Conventional living donor hepatectomy;
Left/right =graft from left or right liver lobe of donors;
TMI= Type for minimally incisions; TCI=Type for conventional incisions;
W = with; W/O = without; Un = unclear or not only one kind; L=Laparoscopic approach; LA=Laparoscopy-assisted; HAL=Hand-assisted laparoscopic;

Comment 3:

- 1) The study show less post-operative complications of donor in MILDH group compared with CLDH. Please describe and discuss why the biliary and vascular complications were less.

Response: We have added the analysis about the postoperative biliary and vascular complications of donors underwent different techniques. All the revision are showed in the part of “Results” and “Discussion”. It is marked with blue font in the revised manuscript.

- 2) Regarding to the complications of donor in each group, it is important to describe in detail even few patients. The reason in each group should be described separately and how to prevent ,especial in MILDH group.

Response: We have added the description of complications in detail. All the revision are showed in the part of “Results” and “Discussion”. It is marked with blue font in the revised manuscript.

- 3) In living donor hepatectomy, the biliary tree manipulation and identification are the key impacts to the functions of graft. The different dissection methods between two groups were also concerned. Please describe the biliary complication in the recipients of each group. The ratio of biliary stenosis is important and it should be compared.

Response: As the processing of biliary tract is crucial for grafts harvested in living donor liver transplantation. And the biliary tree manipulation and identification are the key impacts to the functions of graft. We have perfected our manuscript by adding the analysis of postoperative biliary complications for recipients in detail. All the revision are inserted in the part of “Results” and “Discussion”. We mark the modification with green font in the revised manuscript. We analyzed the included literatures systematically, and found that there were seven studies analyzed postoperative biliary complications for recipients. But not all seven articles classified biliary complications detailedly. Biliary complications in some literature were reported generally, while the rest detailedly. Hence, we do not have sufficient data to analyze the postoperative biliary stenosis separately.

- 4) In the result, there are too many figures to describe just simple event. Please try to use the simple way to show the result.

Response: Indeed, the figures were too much. But all the figures existing were selected deliberately. We thought all the figures were necessary for understanding (to understand) our study. It would affect the integrity of data after deleting some of them.

- 5) For the subgroup analysis, the result and discussion are not coordinated. The result show the operative time is shorter in CLDH (for left hepatectomy) but the discussion described the operative time is similar in

these two groups. What is true? In the discussion, please explain why operative time in left hepatectomy is shorter in CLDH.

Response: In the discussion, the similarity between the two groups referred to the overall result. While in left donor hepatectomy , CLDH group did show shorter operative time than MILDH. Left liver resection, compared to the right lobe or segments resection, was more simple in technical level. Combined with more abundant experience for surgeon groups, conventional living donor left liver resection would take shorter operative time. Frequent replacement of laparoscopic devices would extend operating time for laparoscopic left liver resection in MILDH group. It was worth noting that the operative time for upper abdominal small incision approach in MILDH group was shorter than conventional approaches.