Manuscript NO: 35866
Title: Anterior Versus Conventional Approach Right Hepatic Resection for Large Hepatocellular Carcinoma: A Systematic Review and Meta-analysis
Reviewer's code: 00182114
Reviewer's country: Japan
Science editor: Li-Juan Wei
Date sent for review: 2017-08-15
Date reviewed: 2017-08-17

1. To reduce the risk of bleeding from the anterior wall of the IVC and the transection surface, Belghiti et al proposed the liver-hanging maneuver using a tape passed between the anterior surface of the IVC and the liver parenchyma. The liver is lifted up with a tape during parenchymal transection, and the risk of massive venous bleeding is minimized. Therefore, please write Belghiti's comment in your discussion.

Answers: We highly appreciate the reviewer's valuable comments, we have added Belghiti's comments in the discussion，along with liver-hanging maneuver.

Belghiti et al [33] designed an liver hanging manoeuvre (LHM) using a tape inserted between the anterior surface of the vena cava and the liver and combined it with AA in 2001. The beneficial effects of this technique have been exhibited, including better control of bleeding, protection of the inferior vena cava (IVC), good exposure during deeper parenchymal dissection, and guidelines for the direction of transection [34]. Besides, Chen et al reported a 5-steps stapling technique on right hepatectomy using the anterior approach with the liver hanging technique for patients with hepatocellular carcinoma and liver cirrhosis, and this technique resulted in less intraoperative blood loss, together with significantly shorter time of parenchymal transection. But sometimes it is difficult to control retrograde bleeding when right hepatectomy is used for large HCC, especially in patients with liver cirrhosis and portal hypertension.

2. Please comment bleeding from these branches in patients with liver cirrhosis and portal hypertension to stop in discussion.

Answers: We highly appreciate the reviewer's valuable comments. Generally speaking,

anterior approach was difficult to control the branches of the caudate hepatic vein at the deeper parenchymal transection, especially in patients with liver cirrhosis and portal hypertension. And we have talked about these in the discussion.

Manuscript NO: 35866
Title: Anterior Versus Conventional Approach Right Hepatic Resection for Large Hepatocellular Carcinoma: A Systematic Review and Meta-analysis
Reviewer's code: 01221925
Reviewer's country: Greece
Science editor: Li-Juan Wei
Date sent for review: 2017-08-15
Date reviewed: 2017-08-18

1. How do the authors currently decide which technique to use? Is there a (suggested) algorithm?

Answers: We highly appreciate the reviewer's valuable comments. In our article, patients underwent right hepatectomy in the anterior approach group were associated with less intraoperative blood loss, transfusion requirements and lower mortality, morbidity and recurrence, and better OS and DFS compared with those in the conventional approach group. Thus, we highly recommend the anterior approach for patients with large HCC. However, anterior approach was difficult to control the branches of the caudate hepatic vein at the deeper parenchymal transection, especially in patients with liver cirrhosis and portal hypertension. We recommend the 5-steps stapling technique on right hepatectomy using the anterior approach with the liver hanging technique for patients with hepatocellular carcinoma and liver cirrhosis, because this technique could result in less intraoperative blood loss, together with significantly shorter time of parenchymal transection. Lastly, it is a pity that there is no algorithm in our study.

2. What was the learning curve for the anterior approach at the authors' institution?

Answers: We highly appreciate the reviewer's valuable comments. Our manuscript didn't mention a learning curve in the full text. The purpose of this study was to evaluate the safe and effective technique for right hepatectomy for large HCC. And to date, there was no studies mentioned a learning curve in anterior approach for right hepatectomy.

Manuscript NO: 35866
Title: Anterior Versus Conventional Approach Right Hepatic Resection for Large Hepatocellular Carcinoma: A Systematic Review and Meta-analysis
Reviewer's code: 02438768
Reviewer's country: China
Science editor: Li-Juan Wei
Date sent for review: 2017-08-15
Date reviewed: 2017-08-28

1.Although the theoretical advantages of the anterior approach (AA) over the conventional approach (CA) are well established, right hepatectomy using AA with or without the liver hanging maneuver remains a technically demanding method, making numerous surgeons reluctant to perform this approach. In addition, others see that the CA has the advantage of preventing critical bleeding during liver transection, and the AA can be an effective alternative when difficulty is encountered during liver mobilization. After all, safety should be prioritized when selecting a surgical approach, thus the authors should add these additional topics in the Discussion.

Answers: We highly appreciate the reviewer's valuable comments. We have added your comments into your discussion.

After all, safety should be prioritized when selecting a surgical approach. Although the theoretical advantages of the AA over the CA are well established, right hepatectomy for large HCC using AA with or without the liver hanging maneuver remains a technically demanding method, making numerous surgeons reluctant to perform this approach. In addition, others see that the CA has the advantage of preventing critical bleeding during liver transection, and the AA can be an effective alternative when difficulty is encountered during liver mobilization. In our article, technique of AA was associated with less intraoperative blood loss or massive blood loss, fewer transfusion requirements, lower mortality or morbidity on right hepatectomy. Our results indicated that AA is a safe and effective technique for right hepatectomy for large HCC.

2.Please discuss more the results by adding scientific elements on how AA seems to be safer and more effective technique than CA for right hepatectomy for large HCC than CA when HCC patients with liver cirrhosis and portal hypertension.

Answers: We highly appreciate the reviewer's valuable comments. We have made a further discussion that AA is safer and more effective technique than CA for right hepatectomy for large HCC than CA, especially in patients with liver cirrhosis and portal hypertension.

In our article, we uncovered that technique of AA was associated with less intraoperative blood loss or massive blood loss, fewer transfusion requirements, lower mortality or morbidity, and lower recurrence after right hepatectomy. Furthermore, we also discover a significant association between AA and longer OS and DFS. Besides, Higher incidences of extrahepatic tumor recurrence, alone or in combination with intrahepatic tumor recurrence were detected in the anterior approach than that in conventional approach, and this result seems to support the proposal that excessive blood loss and blood transfusion were associated with increased tumor recurrence, as well as poorer DFS and OS after right hepatic resection. Chen et al reported a 5-steps stapling technique on right hepatectomy using the anterior approach with the liver hanging technique for patients with hepatocellular carcinoma and liver cirrhosis, and this technique resulted in less intraoperative blood loss, together with significantly shorter time of parenchymal transection. But sometimes it is difficult to control retrograde bleeding when right hepatectomy is used for large HCC, especially in patients with liver cirrhosis and portal hypertension.