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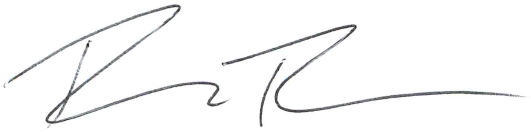
JoVE Submission Review Response

April 23, 2021

To Dr. Bajaj and the JoVE review board,

Thank you for your time and attention given to our submitted manuscript "Robot Assisted Distal Pancreatectomy with Celiac Axis Resection (DP-CAR) for Pancreatic Cancer: Surgical Planning and Technique" (JoVE62232). The thorough and insightful reviews of our work resulted in multiple improvements to our manuscript. We have made the changes and additions, as detailed below and highlighted in the revised manuscript, in response to the reviewers. We sincerely hope these updates make our manuscript suitable for publication and appreciate your time and effort in consideration of our revised manuscript.

Sincerely,



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Reviewer #1

Major Comments:

None

Minor Comments:

1. The authors should add in the introduction with at least one or two references a notion of caution, indeed in some patient the blood flow form the GDA is not sufficient to avoid post-operatory liver ischemia and therefore alternative strategy should be planned as a: pre-operative embolization of the hepatic artery or reconstruction of the coeliac trunk with an interposition graft during the operation.

   Thank you for this pertinent comment. We certainly agree that this anatomical consideration is of merit and should be highlighted in the pre-operative planning stages. We have added a mention of this in our introductory slides discussing potential pre-surgical interventions and intra-operative alternatives to consider.

Reviewer #2

Major Comments:

1. Pathology revealed a mod. diff. T1c PDAC (pancreatic ductal adenocarcinoma). According to the newest staging system for pancreatic cancer, AJCC (American Joint Committee on Cancer) 8th edition (and also earlier editions) tumors are graded T4 if it involves CA (celiac axis), SMA (superior mesenteric artery) and/or CHA (common hepatic artery). In the presented case with a T1c tumor there is per definition no involvement of the CA and therefore no need to resect it. This patient could/should have been treated with at regular distal pancreatectomy.

   Thank you for this pertinent comment. In this patient, the pre-treatment imaging was concerning for involvement of the celiac axis. Further, during operative dissection, there was no safe plane of division between tumor and celiac artery. The final pathology likely reflects favorable response to preoperative chemotherapy. To more clearly illustrate this, we have added pretreatment imaging that shows celiac axis involvement of the tumor. Based on the imaging, we chose DP-CAR as our best chance for margin-negative resection with concern that standard distal pancreatectomy would have a high chance of positive resection margins.

2. The LGA (left gastric artery) is resected. But why? It is not always involved in tumors that require DP-CAR resections.

   Thank you for your comment; we did not choose the correct verb. In the revised manuscript and video we have clarified that the left gastric artery is divided

close to its origin at the celiac trunk, not resected. This allows for maximal collateral blood flow to the stomach through the right gastric.

3. The coronary vein and IMV (inferior mesenteric vein) are both ligated, but why? There is no involvement of mesenterico-portal vein, why it most likely would be possible to spare the coronary vein and for sure the IMV.

Thank you for this comment and we agree sparing both coronary vein and IMV are sometimes possible. In some cases, the IMV inserts into the splenic vein close to the area of planned splenic vein ligation and therefore IMV ligation is required for safe conduct of the operation. We have clarified in the revised video and manuscript, that IMV ligation was not required for the current case as it entered directly into the portal vein. The coronary vein in this case was anterior to the dissection plane needed to identify the arterial anatomy, and ligation facilitated exposure of the arterial anatomy and retroperitoneum.

4. I think there is a general mistake/danger in the described approach to DP-CAR. In pancreatic cancer surgery it is essential to achieve R0 resektion (radicality). When tumors (most often located in the body of pancreas) involve CA a major concern is achieving a tumor free resection margin on the central part of CA (and the plexes surrounding it). Therefore I think it is preferable to address this area very early in the procedure and optimal doing frozen sections from this area before dividing CHA and pancreas ("point of no return"). This can be done robot assisted, but is more complicated.

Thank you for your insight and comments. We agree that R0 resection is of critical importance and that the robotic DP-CAR is facilitated by an inferior to superior approach, which makes assessment of the celiac at the start of the procedure difficult compared to open. To account for this, we rely heavily on the pre-operative CT scan to determine the likelihood of achieving a negative margin at the origin of the celiac axis. Additionally, we take the celiac axis right at its origin along the aorta to maximize the rate of margin negative resection. As you state, if preoperative imaging suggested any tumor involvement at the origin of the celiac axis, a different operative approach would be needed and many patients in that scenario are not resectable. We have added more to the manuscript to demonstrate the potential need to change the approach based on imaging or intra-operative findings encountered at the time of surgery, emphasized the critical importance of pre-operative imaging, and discussed this critical difference in the robotic versus open approach to DP-CAR.

<u>Minor Concerns:</u>

1. line 65 states: "The robotic platform offers numerous technical advantages compared with open and laparoscopic techniques", but the only mentioned advantages are the ones compared to laparoscopic technique: 3D visualization, wrist articulation, multiple instruments... What are the advantages compared with open technique

Thank you for these comments. Indeed, many of the advantages mentioned are related to benefits over laparoscopic surgery. We have added a portion to the manuscript that details that robotic surgery has been suggested to have decreased blood loss, less peri-operative pain, decrease pancreatic fistula rate and faster recovery when compared to open procedures for pancreatectomy in limited case series.

2. Line 94: "..hepatic artery node". I would prefer if the lymph node station was used - the authors probably think of station 8a!?

We have changed the wording in the audio and manuscript to reflect the reviewer's preference for station 8a lymph node.

Reviewer #3:

Major Concers:

1. Authors should include representative images from the preoperative CT scan within the video.

   Thank you for your review. We have added pre and post treatment CT imaging to illustrate more clearly our approach and decision making.

2. I think the video would be aided by including labels for the major anatomical landmarks/vascular structures to help orient the less experienced viewer. The have a nice still image at the end of the video with labels, but including this during the course of the dissection would improve it.

   Thank you for your valuable suggestion. We have added several more still shots of the anatomy to hopefully more clearly highlight relevant anatomy.

3. One thing that is often underemphasized is the importance of mesenteric venous drainage. While in this case, there was no involvement of the portosplenic confluence, the authors should spend time discussing these scenarios; they ligate the coronary vein, which I'm not sure was necessary in this case. But knowledge of coronary venous anatomy (whether it crosses in front of or behind the CHA/SA bifurcation, and whether it inserts into the PV or splenic vein) is critical if there is portosplenic confluence involvement necessitating ligation of the gastroepiploic vein or gastrocolic trunk. Similarly, knowledge of IMV anatomy is important. If both the coronary vein and gastroepiploic vein have to be taken, the patient is at risk of congestive gastropathy and DGE. In this scenario, this Reviewer performs a subtotal or total gastrectomy. These above points should be part of any preoperative planning discussion for the surgeon and consent process of the patient. Important to highlight this for the reader/viewer.

   Thank you for this review and highlighting the importance of anatomical considerations and careful preoperative imaging review that need to be made in

preparation for this case. In our approach, the coronary vein is divided to facilitate arterial and retroperitoneal exposure for further dissection. As the reviewer points out, gastric ischemia and congestive gastropathy and concerns for this procedure. While we routinely ligate the short gastrics and coronary vein, we are careful to spare the gastroepiploic vessels and therefore do not perform a gastrectomy preformed as part of this particular procedure. However, we are careful to check for ischemic changes/congestion to the stomach and liver following resection as was highlighted in the video. However, as suggested by this reviewer, we have added to the pre-operative planning stages in the revised manuscript to address the notion that anatomical aberrancies must be carefully evaluated for and considered prior to planning surgical approaches.

Reviewer #4:
Major Concerns:

1. Dissection of the upper pancreatic border and left gastric artery are missing in the video and should be added.

Thank you for you review and attention to this. We have added video detailing these steps of the procedure.

2.The procedure can be performed with 4-5 ports as well. His should be stated more clearly in the manuscript. Seven ports seems excessive...

Thank you for this insight. We utilize four robotic ports, two assistant ports and a liver retractor for this procedure and for robotic pancreatoduodenectomy. However, there are certainly other approaches that have been demonstrated to be successful. We have added a portion to manuscript and video narrative detailing that alternative port placements can be considered.

3. The authors should include preoperative imaging in the manuscript.

Thank you for this review. We have added imaging from pre-operative CT to the video.

4. Locally advanced PDAC of the tail is treated using anterior or posterior RAMPS in most centres. The authors used a "conventional" distal pancreatectomy. They should at least discuss RAMPS and their rationale for not using it.

Thank you for your insightful review. We have added a discussion of RAMPS approach to distal pancreatectomy to our manuscript.

5. Histology lacks the reported CRM status. Lymph node stations 14a and 16 were not removed during the procedure. Why?

Thank you for this insightful review. CRM was negative and has been added to the pathology report. As for the lymph node stations, these were taken en bloc with the resection and sampled.

Minor Concerns:

1. Preoperative FOLFIRINOX and Radiation therapy are mentioned as "Standard of care". The authors should phrase this more carefully since neoadjuvant chemotherapy is not fully evaluated in prospective trials for PDAC. Radiotherapy is rarely used in Europe to treat pancreatic cancer.

Thank you for this correction. We have changed the wording to more accurately reflect the decision-making process.