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Robot Assisted Distal Pancreatectomy with Celiac Axis Resection (DP-CAR) for Pancreatic Cancer: Surgical Planning and Technique

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TITLE:

Robot Assisted Distal Pancreatectomy with Celiac Axis Resection (DP-CAR) for Pancreatic Cancer: Surgical Planning and Technique

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SUMMARY:

We present our operative approach to robot assisted distal pancreatectomy, splenectomy, and celiac axis resection (DP-CAR), demonstrating that the procedure is safe and feasible with proper planning, patient selection, and surgeon experience.

ABSTRACT:

Malignant pancreatic tumors involving the celiac artery can be resected with a distal pancreatectomy, splenectomy and celiac axis resection (DP-CAR), relying on collateral flow to the liver through the gastroduodenal artery (GDA). In the current manuscript, the technical conduct of robotic DP-CAR is outlined. The greater curve of the stomach is mobilized with care to avoid sacrificing the gastroepiploic vessels. The stomach and liver are retracted cephalad to facilitate dissection of the porta hepatis. The hepatic artery (HA) is dissected and encircled with a vessel loop. The gastroduodenal artery (GDA) is carefully preserved. The common HA is clamped and triphasic flow in the proper HA via the GDA is confirmed using intra-operative ultrasound. A retropancreatic tunnel is made over the superior mesenteric vein (SMV). The pancreas is divided with an endovascular stapler at the neck. The inferior mesenteric vein (IMV) and splenic vein are ligated. The HA is stapled proximal to the GDA. The entire specimen is retracted laterally with further dissection cephalad to expose the superior mesenteric artery (SMA). The SMA is then traced back to the aorta. The dissection continues cephalad along the aorta with the bipolar energy device used to divide the crural fibers and celiac nerve plexus. The specimen is mobilized from the patient‘s right to left until the origin of the celiac axis is identified and oriented towards the left. The trunk is circumferentially dissected and stapled. Additional dissection with hook cautery and the bipolar energy device fully mobilizes the pancreatic tail and spleen. The specimen is removed from the left lower quadrant extraction site and one drain is left in the resection bed. A final intra-operative ultrasound of the proper HA confirms pulsatile, triphasic flow in the artery and liver parenchyma. The stomach is inspected for evidence of ischemia. Robotic DP-CAR is safe, feasible and when used in conjunction with multi-modality therapy, offers potential

for long-term survival in selected patients.

INTRODUCTION:

Pancreatic cancers involving the body and tail of the pancreas are traditionally surgically managed with a distal pancreatectomy and splenectomy. Approximately 30% of pancreatic cancers present in a locally advanced stage with involvement of structures beyond the pancreas[1]. A subset of these patients presents with involvement of the celiac axis or proximal hepatic artery without involvement of the aorta. In this circumstance, an aggressive pre-operative strategy involving neo-adjuvant chemotherapy of FOLFIRINOX[2,3] or Gemcitabine-Abraxane[4] with potential neoadjuvant radiation prior to surgical resection with a modified version of the original Appleby procedure is considered[5]. The procedure involves resecting the celiac axis at its origin and relying on collateral flow to hepatic artery proper through the GDA. While this aggressive approach for locally advanced pancreatic cancer is performed only in highly selected patients, there is suggestion of potential oncologic benefit in retrospective series[6,7,8].

The robotic surgical platform offers numerous technical advantages compared with open and laparoscopic techniques, including enhanced three-dimensional visualization, instrument wrist articulation and the ability for the operating surgeon to control multiple instruments and the camera. Additionally, limited retrospective case series of patients undergoing robotic pancreatic surgery have suggested decreased intra-operative blood loss, decreased peri-operative pain, lower pancreatic fistula rates and improved recovery when compared with open pancreatic resections[9-14]. These technical and clinical benefits along with increased robotic training have led to an expansion of the robotic approach in pancreatic surgery, demonstrating the versatility of the platform to perform a variety of pancreatic resections and procedures, including pancreaticoduodenectomy and distal pancreatectomy with and without splenic preservation. Herein, we will attempt to provide the pre-surgical and surgical evaluation and decision making that is involved in proper selection of patients as well as detail the patient characteristics, pre-operative management, and a detailed review of the surgical technique of the DP-CAR performed with the robotic platform on a singular patient in our practice.

PROTOCOL:

All aspects of this protocol fall within our institutions ethical guidelines of the human research ethics committee

1. Pre-operative planning

1.1. Evaluate the patient pre-operatively.

NOTE: Patients present generally with vague abdominal complains and will be diagnosed primarily by imaging studies. This patient is a 65 year old Caucasian female presented with vague abdominal pain and underwent several CT imaging studies, eventually resulting in a diagnosis of pancreatic mass involving the body of the pancreas and abutting the common hepatic and splenic arteries (**Figure 1**).

1.2. Preoperative Imaging and Biopsy

1.2.1. Proceed initially with cross-sectional imaging to diagnose the mass and identify anatomical relationships, arterial/venous involvement, and any aberrant arterial and venous anatomy. Once identified, proceed with biopsy for tissue diagnosis, if the mass is accessible. This patient's lesion was biopsied during EUS and confirmed as pancreatic ductal adenocarcinoma.

1.2.2. Carefully note and consider any aberrant arterial anatomy or portosplenic confluence aberrancies and involvement of additional structure outside of the celiac axis prior to pursuing surgical resection.

1.3. Consider preoperative therapy .

NOTE: Many different preoperative treatment protocols are available for treatment of locally advanced pancreatic cancer. Patient tolerance and standards of practice at various institutions can guide therapy. In the case of our patient, she was initially started on FOLFIRINOX, but after significant intolerance requiring hospitalization, she was ultimately transitioned to gemcitabine/nab-paclitaxel and completed 6 months of treatment.

1.4. Repeat imaging and serum studies.

1.4.1. Consider follow up imaging to evaluate treatment response prior to moving forward with resection. Serum studies, such as CA 19-9, will additionally help evaluate treatment response. In our patient, imaging demonstrated a promising treatment response as well as a 94% reduction in her serum CA 19-9 levels. However, she continued to have persistent soft tissue infiltration of her celiac axis on repeat imaging (**Figure 2**). As a result, she was scheduled for a robotic DP-CAR.

2. **Initial Operative Steps: Diagnostic Laparoscopy and Robot Docking**

2.1. Begin with a diagnostic laparoscopy to ensure no evidence of metastatic disease.

2.2. Once no **metastatic** disease is confirmed, place the remainder of the ports and dock the robot from the right side of the operating table.

NOTE: Several variations of port placement have been successfully utilized. However, our approach utilizes 4 robotic ports across the upper abdomen, two assistant ports and a liver retractor. A skilled bedside assistant is critical to successful completion of the procedure, utilizing the two assistant ports for operating the bipolar vessel sealing device, suction, and endovascular stapler.

3. **Robot-Assisted Dissection**

3.1. Open lesser sac and mobilize stomach along greater curve.

3.1.1. Following robot docking, proceed with opening the lesser sac with electrocautery and bipolar vessel sealer.

3.1.2. Completely mobilize the greater curve of the stomach with care to avoid sacrificing the gastroepiploic vessels (**Figure 3**).

3.1.3. Cauterize the short gastric arteries with vessel sealing device to the level of the diaphragm. Then retract the stomach and liver edge cephalad to allow for dissection of the porta hepatis.

3.2. Identify hepatic arterial anatomy and assess for adequate retrograde flow into proper hepatic artery and distal liver through the gastroduodenal artery.

3.2.1. After cephalad retraction of the stomach and liver, identify the porta hepatis. Dissect and isolate the hepatic artery node (Station 8a) for removal and permanent pathological evaluation.

3.2.2. At this time, carefully dissect and identify the gastroduodenal artery (GDA). Evaluate for adequate retrograde flow through the GDA into the hepatic circulation with intra-operative Doppler ultrasound.

3.2.3. Identify pulsatile flow in the liver and GDA before and after clamping of the common hepatic artery (**Figure 4**).

3.3. Dissect the inferior border of the pancreas and create a retropancreatic tunnel.

3.3.1. After identification of adequate retrograde flow through the GDA, dissect along the inferior border of the pancreas. Continue dissection with electrocautery and bipolar vessel sealer to identify the superior mesenteric vein.

3.3.2. Create a retropancreatic tunnel over the vein with a sufficient margin from the tumor (**Figure 5**).

3.4. Divide the pancreas and continue the retropancreatic dissection to divide the splenic vein and coronary vein.

3.4.1. Divide the pancreas with an endovascular stapler. Mobilize the inferior and posterior border of the pancreas laterally with electrocautery and bipolar assisted dissection.

3.4.2. Divide the splenic vein and coronary vein to assist in visualization of arterial anatomy and retraction. Additionally, the inferior mesenteric vein may be ligated if it inserts laterally into the splenic vein.

3.5. Divide the hepatic artery and expose the superior mesenteric artery.

3.5.1. Turn attention back to the hepatic artery and continue dissection to fully delineate the anatomy if required. Divide the hepatic artery proximal the gastroduodenal artery (**Figure 6**).

3.5.2. Once the hepatic artery is divided, retract the specimen laterally and continue to mobilize the pancreas to expose the superior mesenteric artery (SMA).

3.6. Identify and trace the superior mesenteric artery to its root on the aorta.

3.6.1. Once the SMA is identified, dissect cephalad along the superior border to trace it back to the origin on the aorta (**Figure 7**). Continue the dissection cephalad with electrocautery and bipolar cautery through dense connective tissue.

3.7. Dissect cephalad from the root of the SMA through dense connective tissue, nerve bundles, and lymphatic tissue until muscle fibers from the diaphgramatic crura are identified.

3.7.1. During this en bloc mobilization of the tissue overlying the superior mesenteric artery and celiac axis as well as the final lateral dissection, sample lymph node stations 14, 16 and 18.

3.8. Ligate the left gastric artery near its origin with an endovascular stapler to maximize collateral blood flow to the stomach.

3.9. Expose and divide the celiac axis.

3.9.1. Continue retracting the sample to the patient's left and dissect through the crural muscle fibers until the origin of the celiac axis is visualized (**Figure 8**). It is of utmost importance to maintain sufficient lateral retraction on the specimen to rotate the celiac axis to the left of the patient. This will facilitate ligation of the celiac trunk by providing a favorable angle for the endovascular stapling device.

3.10. Continue retroperitoneal dissection laterally to fully mobilize pancreas and spleen and remove specimen.

3.10.1. Continue the retroperitoneal dissection laterally with a combination of hook and bipolar cautery. Remove the specimen through the left lower quadrant incision, which can be extended if necessary. A detailed view of the final resection bed vascular anatomy is available in the supplementary figures (**Figure 9**).

3.10.2. Complete a final intra-operative ultrasound of the proper hepatic artery continues to demonstrate pulsatile, triphasic flow in the artery and parenchyma of the liver. Evaluate the stomach for external signs of ischemia.

3.10.3. Once a final inspection is completed, undock the robot, and close the fascia and skin. The procedure is complete.

REPRESENTATIVE RESULTS:

The duration of the procedure was 228 minutes with a blood loss of 50 mL. Post-treatment final pathology revealed a moderately differentiated (G2) ypT1c ductal adenocarcinoma. No nodal involvement was noted (0/21 total nodes). The circumferential resection margin was negative. The patient's post-operative course was uncomplicated. Her drain amylase levels post-operatively were in the normal range and the drain was removed on post-operative day 3. She was discharged home on post-operative day 4 tolerating a regular diet. Her follow appointments in clinic demonstrated that her recovery was progressing well.

Figure 1: Pre-treatment CT imaging demonstrating locally advanced body of pancreas mass involving celiac axis and splenic vein.

Figure 2: Post-treatment CT imaging demonstrating locally advanced body of pancreas mass involving celiac axis and splenic vein with persistent soft tissue infiltration surrounding celiac cells.

Figure 3: Opening of lesser sac and mobilization of greater curve. Short gastric vessels are ligated with care taken to preserve gastroepiploic vessels.

Figure 4: Dissection of porta hepatis with identification of common and proper hepatic artery and gastroduodenal artery with triphasic ultrasound signal.

Figure 5: Dissection of inferior border of pancreas with identification of superior mesenteric vein and creation of retropancreatic tunnel overlying vein.

Figure 6: Final identification of arterial Following division landmarks and adequate flow prior to ligation of common hepatic artery.

Figure 7: Following division of pancreas, the superior mesenteric artery is exposed and dissection proceeds cephalad to its root on the aorta.

Figure 8: Celiac axis origin exposed and oriented to patient left by laterally retracting the specimen prior to division.

Figure 9: Final resection bed anatomy highlight.

DISCUSSION:

With proper pre-operative planning, patient selection, and surgeon experience, it is clinically feasible and safe to approach locally advanced pancreatic tumors of the body/tail of the pancreas with celiac involvement with robot assisted distal pancreatectomy, splenectomy, and celiac axis resection. Proper patient selection requires comprehensive pre-operative planning with cross-sectional imaging to identify the tumor and its anatomical relationship to surrounding vascular structures. At this time, it is also imperative to identify any anomalous arterial or venous circulation that would imperil attempted resection or make it infeasible.

Intra-operative findings may also shift our treatment approach in real time. Findings suggesting the continued involvement of the celiac root at the time of surgery would make resection infeasible. Therefore, high quality post-treatment imaging prior to surgery is also critically important to evaluate the degree of treatment response. Additionally, findings on inadequate retrograde arterial flow through the gastroduodenal artery to the proper hepatic artery or distal liver parenchyma may require an arterial reconstruction, and pre-operative preparedness for this reconstruction is imperative. After resection, gastric ischemia or congestion due to division of major vascular structures is a potential and morbid sequela. However, despite division of the short gastric vessels and left gastric artery, the gastroepiploic circulation remains unviolated in the course of this dissection. These vessels are often adequate to ensure adequate perfusion of the stomach and therefore gastrectomy can be avoided. However, the stomach must be observed closely for ischemic changes prior to conclusion of this procedure.

The traditional operative approach to management of tumors involving the body and tail of the pancreas is a distal pancreatectomy. However, more recently, radical antegrade pancreaticosplenectomy (RAMPS) has been proposed as an alternative procedure that is increasingly utilized and has been suggested to offer an increased rate of negative tangential margins[15]. Despite these promising results, no large prospective studies yet exist that show a demonstrable improvement in overall survival or recurrence free survival when compared with traditional distal pancreatectomy. Additional prospective studies are needed to establish clear clinical guidelines for routine use of RAMPS during distal pancreactomy[16].

The robot platform has seen ever increasing use in a variety of complex pancreatic resections. This protocol and video highlights one potential operative approach utilizing this platform for approaching a clinically challenging disease process.

ACKNOWLEDGMENTS:
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The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

DISCLOSURES:
No financial conflicts of interest to disclose on the part of any of the authors involved.

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Figure 1. Pre-treatment CT imaging demonstrating locally advanced body of pancreas mass involving celiac axis and splenic vein.

Figure 2. Post-treatment CT imaging demonstrating locally advanced body of pancreas mass involving celiac axis and splenic vein with persistent soft tissue infiltration surrounding celiac axis

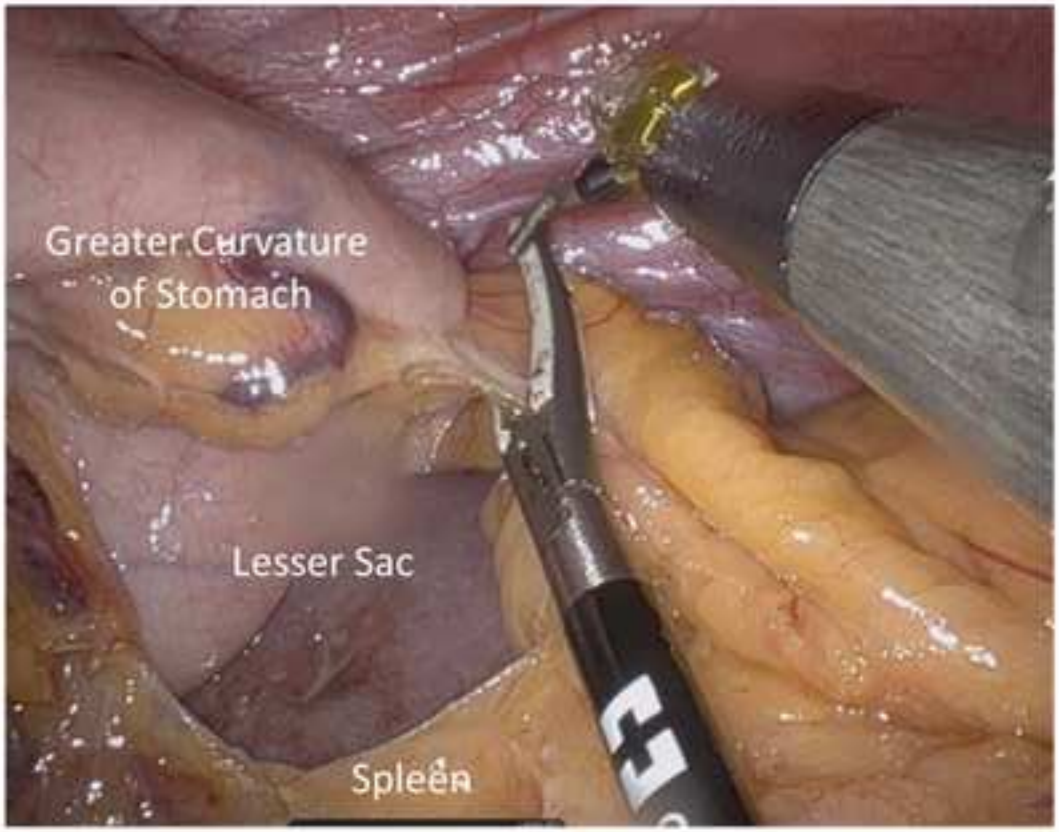

Figure 3. Opening of lesser sac and mobilization of greater curve. Short gastric vessels are ligated with care taken to preserve gastroepiploic vessels.

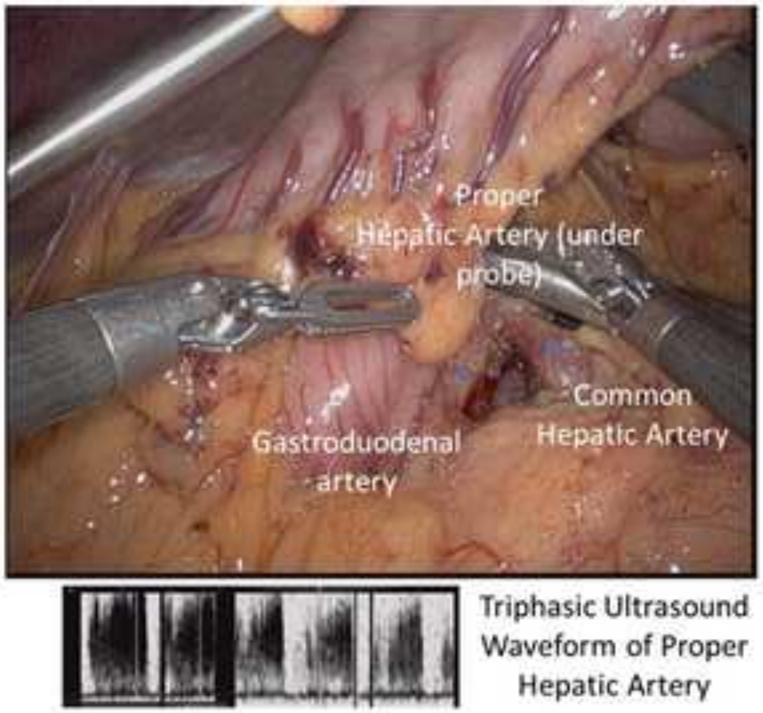

Figure 4. Dissection of porta hepatis with identification of common and proper hepatic artery and gastroduodenal artery with triphasic ultrasound signal

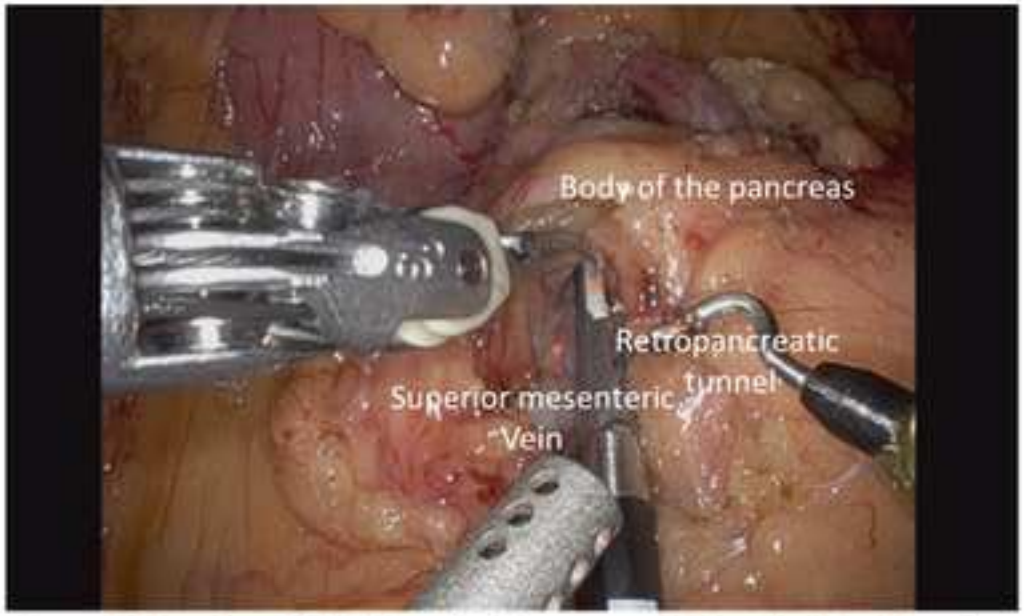

Figure 5. Dissection of inferior border of pancreas with identification of superior mesenteric vein and creation of retropancreatic tunnel overlying vein.

Figure 6

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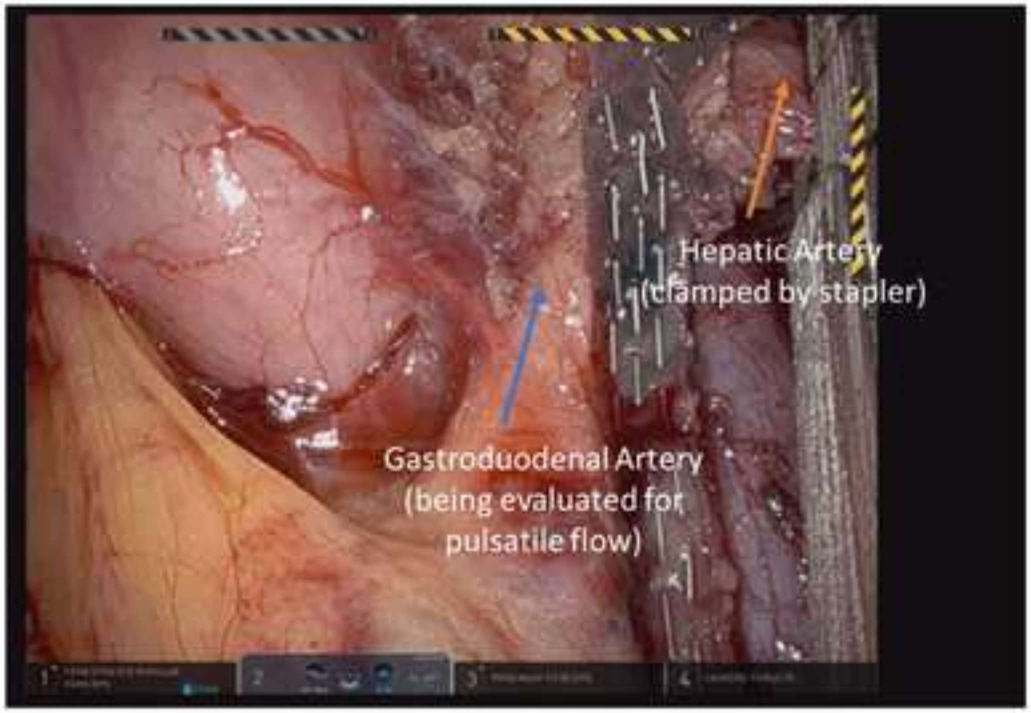

Figure 6. Final identification of arterial landmarks and adequate flow prior to ligation of common hepatic artery.

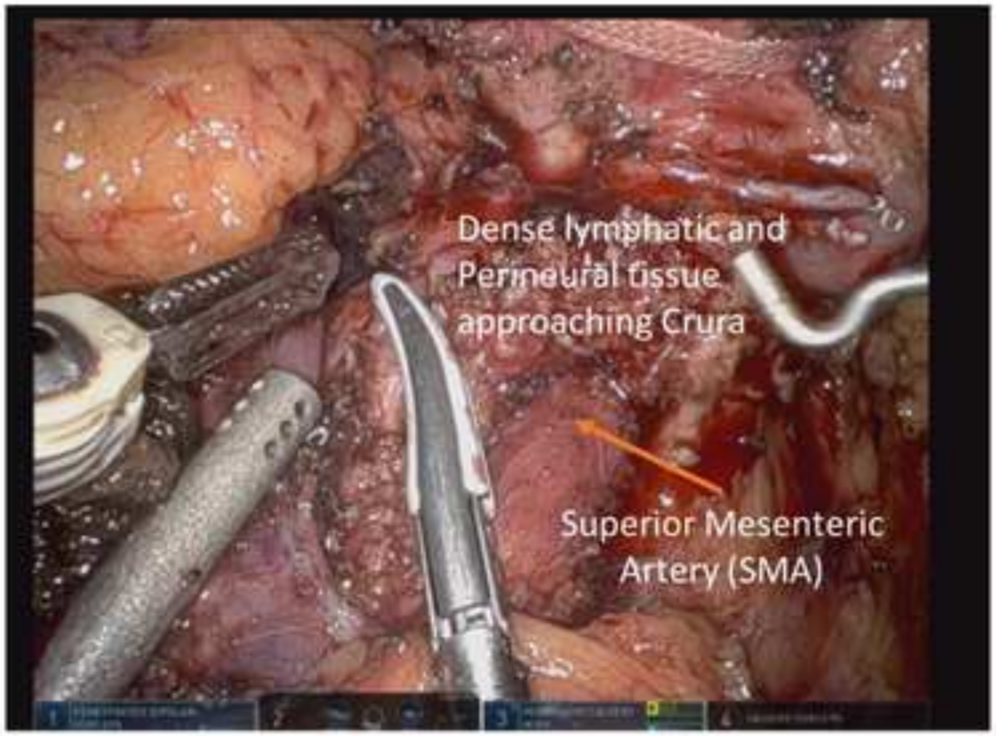

Figure 7. Following division of pancreas, the superior mesenteric artery is exposed and dissection proceeds cephalad to its root on the aorta

Figure 8

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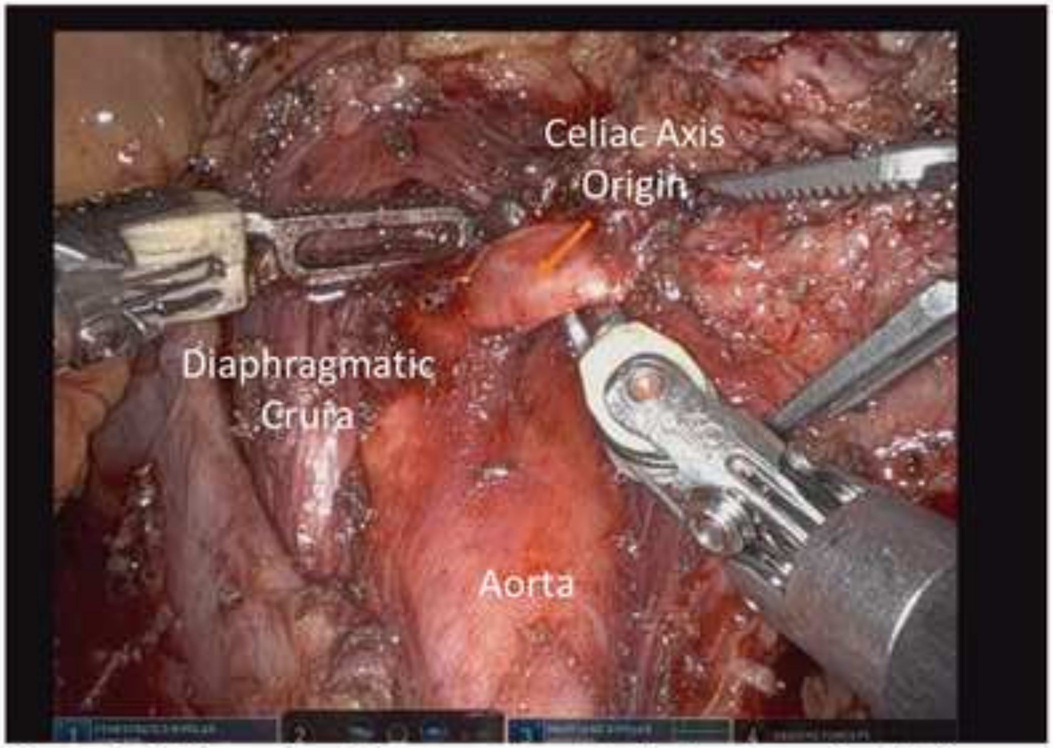

Figure 8. Celiac axis origin exposed and oriented to patient left by laterally retracting the specimen prior to division

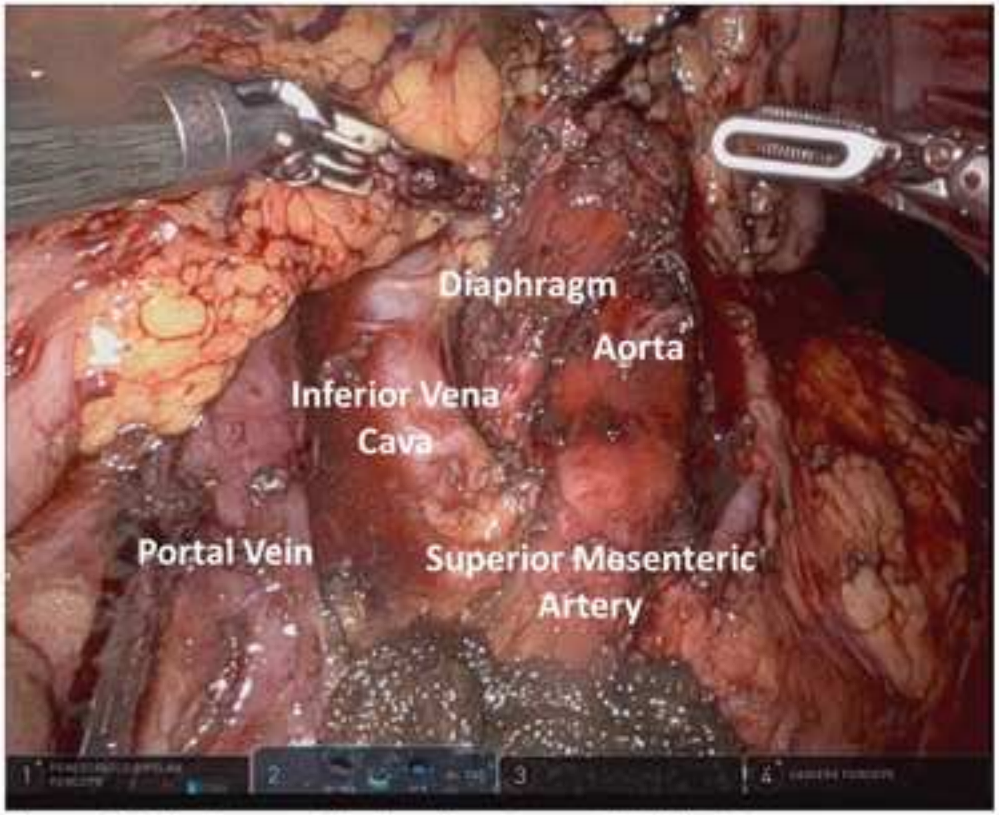

Figure 9. Final resection bed anatomy highlight

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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.

Minor Concerns:

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.

<u>**Reviewer #3:**</u>

<u>**Major Concers:**</u>

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.

<u>Minor Concerns:</u>

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.