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Name of Journal: ***World Journal of Gastrointestinal Surgery***

ESPS Manuscript NO: 25636

Manuscript Type: ORIGINAL ARTICLE

April 27, 2016

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Scientific Editor
World Journal of Gastrointestinal Surgery

Reply to 1st reviewer comments:

1-We have added this recent manuscript to our references, and add this comment of the reference in our discussion.

2- This is clarified within the text. We mean to say that emergent TP was not used as a treatment for POPF for those in whom this developed after undergoing partial pancreatectomy.

3- In our results of 20/42 patients with recurrent PDAC the mean time of recurrence was 9.5 months (range = 2.5-27 months). 5 patients underwent completion TP for recurrent PDAC. Early recurrence is rare in this current era due to improved imaging but due to the time frame of this study, there were a very small number of patients who developed distant metastatic disease within 6 months of the operation.

4-Table 1 gives the overall results of the study (n=104) and give the demographic for the three most interesting a largest subgroups found within the overall study (patients with PDAC, IPMN, or undergoing LTP). This subgroup analysis was given so that the reader may investigate further into any one of these subgroups if they desired. PDAC may develop within IPMN but not always. Similarly, not all IPMN has associated PDAC. The "IPMN" group is all of those found to have benign IPMN changes. The PDAC group includes all of those who were found to have invasive adenocarcinoma whether it developed de novo or within IPMN changes. We did not give the demographics of those undergoing open total pancreatectomy or those

undergoing TP for pathology other than PDAC or IPMN as these subgroups were not a focus of any of the subgroup analyses.

5-Correct, there were no cases were ASA I.

6- No, islet autotransplantation was not considered for the 8 patients undergoing TP for benign causes. These patients had concern for neoplastic disease and islet autotransplantation was not indicated. Those with indications for islet autotransplantation are referred to another institution.

Reply to 2nd reviewer comments:

1. Clarify what is your definition of high volume centre and add this.

It is a tertiary referral center for pancreatic diseases and we perform over 100 major pancreatic procedures/year.

2. I completely disagree that any sound mind HPB surgeon would do TP during planned PD due to soft pancreas as claimed in introduction paragraph. It is criminal to certain extent. People in general modify techique or just do same technique BUT dont go to the extent of TP unless oncology demands. So erase that part.

Agreed. This is a historical indication for TP and it will be removed to avoid offending any readers.

3. I disagree that R2 resection for IPMN is OK. You quote your own paper and justify again! Cummon, do you believe this yourself? Is this based on sound evidence, if so what level and grade? Such bold statements will mislead weak

readers of journals and they will start believing that R2 is ok. Do you want that message?

In our study, there were no cases with R2 for IPMN. There was only 1 case of R2 resection after TP for PDAC of a margin involving the SMA in this study (as well as our previous reference). This was performed many years ago by surgeons not involved in this study and we agree, this is not an ideal situation and we would not perform a TP for a patient with a positive margin at another location under our current practice. The data and conclusion from the other study referenced (#34) will be removed to assure that there are no mixed messages.

4. 40% vein resection for PD. How many histology were invasion seen in vein? We all know Prof Cameron experience about 95% desmoplasia and not invasion and resection is overdone. Whats your data and eperience?

Unfortunately, data regarding actual histological vein invasion is not available. We agree that it is likely that not all of those patients undergoing vein resection had actual invasion and aggressive venous salvage techniques are currently used at our institution.

5. Do we need survival for benign disease? Is the cause of death related to pancreas disease or other disease?

We believe that survival after TP even for benign disease is an important emphasis of study. The creation of complete endocrine and exocrine insufficiency of the pancreas by TP can cause significant complications and even death and therefore the study of patient survival after TP for benign disease is worthy of investigation and inclusion in this study.

6. Why were IPMN operated? What is preop work up and what diagnostic criteria used? What management criteria used?

Preoperative diagnosis was based on the findings of computed tomography and/or magnetic resonance imaging and magnetic resonance cholangiopancreatography. Most of the patients also underwent endoscopic ultrasound (EUS) with or without fine needle aspiration. The IPMN may be main, mixed, or branch duct IPMN based on the diameter of the main pancreatic duct, according to the 2012 consensus guidelines. Each case may had findings of high-risk stigmata or worrisome features and the

management criteria used was based on the updated guidelines as written below and added to the manuscript.

Tanaka M, Fernandez-del Castillo C, Adsay V, et al. International consensus guidelines 2012 for the management of IPMN and MCN of the pancreas. Pancreatology 2012;12:183-197

7. You mention 2008 onwards protocol is established. What is this protocol? We need readers to know that.

Around this time period, we established perioperative care pathways that mainly involved patient undergoing preoperative nutritional and endocrine counseling regarding their postoperative condition. In addition, jejunostomy feeding tubes were placed as a routine during the performance of TP. This information was added to the manuscript.

8. Unclear is any of your TP pts had auto islet transplant?

No, these patients were referred to other specialized centers for this procedure (see above).

9. How do u manage enzyme replacement therapy? What is your protocol. Your paper needs this information. Op time blood loss Los morbidity etc is routine and honestly not of any value in a broad sense. Readers would want to know how do you manage perioperTively?

Postoperative enzyme replacement was instituted beginning when the patient begins to take in oral intake. There was no specific protocol regarding this and the enzyme dosing was adjusted based on the patient's needs and po intake. Additional information regarding this is added to the manuscript.

10. Tell readers about ICU stay, perioperative TPN use, transfusion needs and trigers, preoperTive optimization and assessment, adjuvant therPy protocols etc.

This was included in the methods section.

11. 90 day mortality of 6.8% and 1 year survival appx75%. What happens between 3 months to 1 year that 20% die? This is very intereting especially for benign pathology patients. This needs major discussion.

The 1 year survival after TP is affected by many things. 90 day mortality, even in high volume centers, is higher than seen for PD in literature mainly due to the increased medical and surgical complications. Similarly, it stands to reason that the 1 year survival will also be found to be lower than that seen

for PD. Unfortunately, medical complications and aggressive neoplastic pathology will likely cause a higher mortality than ideal in the short and long term after TP. In recent years, improvements in preoperative imaging and staging have decreased those experiencing early disease recurrence and improvements in postoperative endocrine & exocrine insufficiency have decreased those experiencing life threatening medical complications in the first year postoperatively. This has resulted in better 1 year survival in recent years. However, this is a retrospective study spanning 20 years and the purpose of this study is to report historical outcomes that unfortunately, cannot be changed.

12. Define major glycemic event. 13. Why pt had hepatic insufficiency? 14. Clarify type of cardiac and pulmonary comorbidity?

This was clarified in the methods.

15. Renal cell cancer, sarcoma etc cases TP wa done. Such cases need sepRTe discussion too.

These were unusual cases involving multifocal recurrent renal cell cancer and sarcoma involving the head of the pancreas with agenesis of the tail. Also included were several other patients with neoplastic disease of the head of pancreas and associated IPMN changes within the pancreas requiring TP. We focused the manuscript on the subgroups of interest (LTP, PDAC, and IPMN) and did not devote manuscript space to discuss these unusual cases.

16. Show only curvez of pdac and ipmn separately.

This analysis was performed and added to the manuscript in figure form.

17. Is it right to assume that IPMN in patient with PDAC - PDAC came from IPMN? Can they not be coincidental? Whats evidence here. Thanks

Yes, PDAC-IPMN patients were found to have PDAC develop within IPMN and not coincidental.