

Response to reviewers' comments

The authors thank the reviewers' for the positive and constructive comments.

Reviewer #1:

1. *The line spacing is different in many places in the text.* Addressed

2. *When analyzing OS, many articles divide it into time nodes of 1 year and 3 years, because other factors will also affect the accuracy of OS. For example, like PALN, the neurological invasion phenomenon greatly affects the prognosis. It has been documented that LN metastasis can trigger PN invasion, which may lead to peritoneal dissemination and a higher recurrence rate. Perineural infiltration is the only prognostic factor for 3-year OS. But in this article, these are not explained. 3- and 5-year survival rates are another way of presenting the data. The authors opted for median overall survival with range to better present the OS and the minimum and maximum observed values. Indeed other factors affect survival, such as perineural and periarterial invasion. These parameters have been included in the risk analysis for both OS and DFS to investigate which are the independent prognosticators. The results are clearly presented with perineural invasion been identified as an independent predictor for DFS.*

3. *The patient's treatment range and whether to use chemotherapy (neoadjuvant chemotherapy or adjuvant chemotherapy) are related to many indicators, such as Tumor size, tumor location, and scope of invasion and so on. This article does not elaborate but directly summarizes the conclusions.* Based on the NCCN guidelines there is limited evidence to recommend specific neoadjuvant regimens. With regards to adjuvant treatment the pathological characteristics such tumour location, size etc cannot definitively influence the decision for the type of regimen which is also affected by the performance status of the patient and any post-operative complications. The NCCN guidelines suggest modified FOLFIRINOX or gemcitabine-based regimens. These depend on institutional practice. Our study covered a long period during which chemotherapy practice has changed following the results of relevant trials. In the early part of the study gemcitabine-based regimens were used both in the neoadjuvant and adjuvant setting for all patients with PDAC. In the later years of the study, the preferred regimen was modified FOLFIRINOX for all patients that could tolerate it and if this was not possible then gemcitabine-based regimens as a second option. This has been clarified in the manuscript. This was already mentioned in the discussion section and has been also added in the methods section of the manuscript.

Reviewer #2:

1. *In the introduction section: the authors should provide more information of the standard for lymphadenectomy (where these lesions?) based on the ISGPS guideline. The recommendations of ISGPS for standard lymphadenectomy have been briefly expanded in the introduction and analysed in more detail in the discussion section of the manuscript: "A consensus statement from the ISGPS suggested that extended lymphadenectomy is not indicated in pancreatic resections (10). The same group defined standard lymphadenectomy for pancreaticoduodenectomy to include lymph nodes in the hepatoduodenal ligament (stations 5, 6, 8a, 12b, 12c), pancreaticoduodenal groove (stations 13 and 17), right side of the superior mesenteric artery (stations 14a and 14b) and for distal pancreatectomy those along the splenic artery (station 11), along the inferior border of the pancreas (station 18) and in the splenic hilum (station 10), with station 9 to be included only in pancreatic body tumours. Resection of PALN (station 16) was not recommended based on the reported poor outcomes of patients with PALN positive disease. Nonetheless, it was acknowledged that PALN may be included in the resection plane based on individual practice."*

2. *In the methods section:*

2.1 *what are the common chemotherapy regimens for PDAC patients in your institute? Our study covered a long period during which chemotherapy practice has changed following the results of relevant trials. In the early part of the study gemcitabine-based regimens were used both in the neoadjuvant and adjuvant setting for all patients with PDAC. In the later years of the study, the preferred regimen was modified FOLFIRINOX for all patients that could tolerate it and if this was not possible then gemcitabine-based regimens as a second option. This was already mentioned in the discussion section and has been also added in the methods section of the manuscript.*

2.2 *What the definition for DFS or OS in this cohort? This has been clarified: "Overall survival was defined as the time from diagnosis to death or last follow-up and disease free survival as the time from resection to diagnosis of disease recurrence"*

The end date for following up these patients? This has been clarified: "Follow-up of patients was determined from time of diagnosis until disease recurrence or death"

3. *In the results section: As you mentioned that only patient had visible PALN metastasis via image? Would you provide the image of this patient? Provided as supplementary material*

4. *In the discussion section: there are more information of different clinical outcomes regarding positive PALN in the discussion section? Would you provide a Table to summarize these findings? All study outcomes are included in the text or tables to avoid repetition.*

5. *There are few grammar errors in the whole manuscript? Addressed*

Reviewer #3:

1. *It is great that you could put DFS in the article. Thank you, the authors appreciate the positive comment*

2. *Why did you not put PALN (+) in multivariable model for overall survival ? One of the main oncological questions is whether PALN+ disease behaves as metastatic or more as pN+ disease in terms of patients' survival. PALN+ was introduced in multivariate models to determine whether it is an independent factor for overall survival.*

3. *You have one case that underwent distal pancreatectomy, why do you put only one case in the data. Furthermore, the lymphatic pathway of the left side of the pancreas is quite different from the pancreatic head. So I think that it might affect the results. There was only one case of distal pancreatectomy where PLAN was sampled during the time period of the study. Indeed the lymphatic drainage of the left side of the pancreas is different, however lymphatic drainage pathways exist between the peripancreatic and splenic hilar LNs (which are the fist port of lymphaativ drainage of the distal pancreas) and the para-aortic LNs.*

4. *Do you have a more detailed information about each LN station, the number of harvested LN, the number of positive LN, LN ratio? The area of PALN sampling is included in the methods section "PALN were sampled from the infra-renal, aortacaval lymph nodes and more specifically from the level of the third part of the duodenum to the angle of the left renal vein", therefore indicating LN station 16. This has been added in the manuscript. The median sampled LNs was 2 (range 1-7) and median positivity ratio 0.5 (range 0.14-1). This has been added in the results section of the manuscript.*

5. *Is there any risks/complications for patient who having PALN sampling? The theoretical post-operative risks for complications, including haemorrhage and chyle leak, have been analysed and included in Table. There was no significant difference with PALN sampling.*

Science editor:

1. *The introduction is not accurate and detailed enough. The author should provide more information on the criteria for lymphadenectomy according to the ISGPS guidelines.* The recommendations of ISGPS for standard lymphadenectomy have been briefly expanded in the introduction and analysed in more detail in the discussion section of the manuscript: “A consensus statement from the ISGPS suggested that extended lymphadenectomy is not indicated in pancreatic resections (10). The same group defined standard lymphadenectomy for pancreaticoduodenectomy to include lymph nodes in the hepatoduodenal ligament (stations 5, 6, 8a, 12b, 12c), pancreaticoduodenal groove (stations 13 and 17), right side of the superior mesenteric artery (stations 14a and 14b) and for distal pancreatectomy those along the splenic artery (station 11), along the inferior border of the pancreas (station 18) and in the splenic hilum (station 10), with station 9 to be included only in pancreatic body tumours. Resection of PALN (station 16) was not recommended based on the reported poor outcomes of patients with PALN positive disease. Nonetheless, it was acknowledged that PALN may be included in the resection plane based on individual practice.”

2. *in the method section: Please provide the specific chemotherapy regimen commonly used by PDAC patients.* Our study covered a long period during which chemotherapy practice has changed following the results of relevant trials. In the early part of the study gemcitabine-based regimens were used both in the neoadjuvant and adjuvant setting for all patients with PDAC. In the later years of the study, the preferred regimen was modified FOLFIRINOX for all patients that could tolerate it and if this was not possible then gemcitabine-based regimens as a second option. This was already mentioned in the discussion section and has been also added in the methods section of the manuscript.

3. *Please make sure that the definition of DFS or OS in this queue is.* Follow-up information about patients is not detailed, such as end date, etc. These have been clarified: “Overall survival was defined as the time from diagnosis to death or last follow-up and disease free survival as the time from resection to diagnosis of disease recurrence” and “Follow-up of patients was determined from time of diagnosis until disease recurrence or death”.

3. *The discussion section is not comprehensive enough.* The discussion has been expanded and especially around the ISGPS consensus.