

1. Inclusion and exclusion criteria should be clearly presented

→ Thank you for your comment. We included patients with pathologically confirmed stage I PDAC who underwent upfront surgery between January 2000 and April 2016. We excluded those with neoadjuvant chemotherapy, obstructive jaundice, and Lewis-antibody negative. We also excluded patient who were lost to follow-up, and who had incomplete data on preoperative serum CA 19-9 levels. These specific criteria are described in methods and shown more schematically in figure 1.

2. table 1 missing patients (not 407), should be mentioned. Ex. two missed in location criteria?

→ Thank you for your comment. I rechecked the table and the data and revised the table and results. The final report revealed that tumor was involved in both head and body in two cases. Histological differentiation in five cases were unknown.

3. results separated with subtitles

Done as mentioned. Thank you.

4. The AUCs for predicting early recurrence were  $<0.7$ , indicating low accuracy. For instance, AUC of CA19-9 was 0.605 and tumor size was 0.619. It would be much better to construct a predictive model with much higher AUC.

→ Thank you for your recommendation. I agree with your opinion. If the AUC had been higher, it would have been much better. However, when referred to previous studies working on cut-off levels, ROC curve was commonly used method, and we thought it also suited for our study. The deviation of CA 19-9 level or tumor size among patients is bound to be small because we included only PDAC 1 stage patients, and we think it could be the reason of low AUC.

1. Kindly provide multivariate analysis using the described variable in early recurrence vs. no group. Table 2 talks about the entire cohort without any mention of early recurrence or no. Based on the findings and results, the conclusion can not be drawn. Most of the references are old and may not be relevant in the current context.

→ Thank you for your comment. In this study cohort, 98 patients had early disease recurrence. Table 2 is about the risk factors of early recurrence using multivariate analysis. And the part that you mentioned

is shown in table 3 which is about the comparison between the early recurrence group and non-early recurrence group.

1. only CA 19-9? What about CEA? CEA included?

→ In this study, we only evaluated preoperative serum CA 19-9 values. In our institution, we also check preoperative CEA value, but CA 19-9 level is the one that is routinely checked postoperatively during surveillance. Postoperative CEA value was missed in many patients.

2. change of CA 19-9 after operation compared with before operation?

→ Thank you for your comment. We had postoperative serum CA 19-9 values checked within a month after the operation. Among 181 patients with preoperative serum CA 19-9 values  $\geq 70$  U/mL, 171 patients (94%) had decreased serum CA 19-9 values after the operation, and of these, 49 patients (28.7%) experienced early disease recurrence. Nine patients had rather increased serum CA 19-9 value and all these patients experienced early recurrence. In one patient, we did not check postoperative CA 19-9 value. I added this information in the results.

3. Inconsistent judgment results caused by different pathologist?

→ A couple of different pathologists made judgement on final biopsy report. However, they made decision based on the definition such as resection margin status which is mentioned in method. Thank you.

4. Which patients received adjuvant chemotherapy after surgery and what are the standards?

→ Thank you for your comment. Basically, all the patients are recommended to have adjuvant chemotherapy regardless of disease stage. However, final decision is made based on the oncologists' decision and patients' postoperative general condition. In our study, patients who were in poor general condition, with postoperative complication, old, or reluctant to chemotherapy did not undergo adjuvant chemotherapy. We added this information in the discussion.