

July 18, 2015

Re: **ESPS Manuscript NO:** 19599

Dear Editor:

We have revised our manuscript "**Features Associated with Progression of Small Pancreatic Cystic Lesions – a Retrospective Study**" according to the reviewers' comment and the journal's format. The changes are highlighted in the revised manuscript and are listed as follows. Thanks for your review and comments to our manuscript.

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(For note, pages and lines listed below are corresponding to the change-highlighted copy of the manuscript.)

Response to Reviewers:

Reviewer 3251601

Q1. Grammatically the abstract could do with re-structuring. Enrolled implies recruited, and perhaps another term can be used instead

Response:

Thanks for reviewer's suggestion. As seen in the page 4, we have revised the abstract. The wording "enrolled" was changed to "evaluated".

Q2. Wording suggestion for core tip: "Surveillance can be associated with." and "Again – perhaps use a different word for lenient"

Response:

Thanks for reviewer's suggestion. However, we deleted these description according to the suggestion of the other reviewer (as below). We have revised the content of core tip.

Page 5: "Observation is advised for small pancreatic cyst without concerning features of malignancy. Our study explored that small pancreatic cysts with borderline pancreatic duct dilation, tubular shape, or septa were associated with risk of

progression. Our findings may be helpful to stratify patients for different management planning according to their risk of progression.”

Q3. Wording suggestion for patients and methods: “Patient selection?”

Response:

Thanks for reviewer’s suggestion. As seen in the page 7, we have added the wording – “selection”.

Q4. I presume that you have targeted your study towards 135 asymptomatic patients without signs or symptoms or pancreatic pathology? – this should be made clear.

Response:

Yes, this study was based on these 135 patients. We have revised the description to avoid confusion.

Page 7, the last line and page 8, the first 3 lines:” Finally, data from the remaining 135 patients with incidentally detected small pancreatic cystic lesions (94 men, 41 women; age range, 20–92 years; mean age, 67 years) were evaluated.”

Q5. Did any patients undergo EUS?

Response:

No, none of our patient underwent EUS. We clarify it in the manuscript.

Page 8, the line 6 to 8: “As none of our patient was associated with concerning features of malignancy, none of them had been studied by endoscopic ultrasonography.”

Q6. Does this level of imaging protocol description add to the scientific content/reproducibility over describing CT as pancreatic protocol/phase etc?

Response:

We describe the protocols of CT and MRI as a routine in writing scientific paper. We added the following sentence for clarity.

Page 8, the 2nd paragraph: Since most of our patients underwent the imaging examination for studying other abdominal disease, the protocols we used were not specific to pancreas disease but were those that we routinely used for abdomen examination.

Q7. Was this using the same imaging modality/different?

Response:

No, the comparison of interval change may not use the same imaging modality. We clarify it in our manuscript.

Page 8, Line 4 – 6: The interval progression was examined by using the initial and the last imaging of cyst and may be not of the same imaging modality.

Q8. These 3 groups are explained below, but they should be introduced in “patients and methods” for clarity.

Response:

We introduce the 3 groups in the section of patient and methods.

Page 10, the section of “Grouping”: We added the following description “Accordingly, the patients were divided into 3 groups: the non-progression, the minimal-change, and the progression group.” for clarity.

Q9: Clarify sentence (in the section of clinical features of results) – needs some minor adjusting to make the point clear

Response:

We re-write the sentence as “The mean age of the progression group was the oldest among the three groups but it was not significantly different from that of the non-progression group” to make the point clear (page 10, the last line 5 to 3).

Q10: Clarify sentence – did more patients have uncinete process cystic lesions?

Response:

No. few patients had uncinete process cystic lesion. We re-write the sentence as: “Few cystic lesions were detected over the uncinete process. The rest of cystic lesions were evenly distributed across all the other sites of the pancreas and there was no predilection site for progressive pancreatic cystic lesion” (page 11, the 2nd paragraph, line 6-8).

Q11: In the section of regression analysis: “This is an odds ratio”

Response:

We correct it as “lesions with septa had 5.318 increased odds of interval progression than lesions without septa” (page 12, line 1-2).

Q12: This sentence should be linked to the following describing the predominance of male patients undergoing abdominal imaging in Taiwan.

Response:

We revise the sentence as: “Since all our cystic lesions were asymptomatic and found incidentally during imaging examinations for abdominal organs other than pancreas, this finding may just reflect the male predominance of liver diseases in this liver diseases endemic country” (page 14, the 3rd paragraph, line 3-6).

Q13: Change word, re-structure sentence: it is dubious that the progression rate of a cystic lesion may not be constant and can be accelerated as the cyst gets larger.

Response:

We revise the sentences as: One may suspected that the progression rate of cyst may not be constant and can be accelerated when the cyst gets larger and questioned at the progression rate of 1 mm/year that was determined by observing cyst progression at different follow-up interval instead of year-by-year (page 14, the last paragraph and page 15, the first paragraph).

Q14: Consider using a different term other than “lenient”.

Response:

We change the wording to “relaxed”.

Reviewer 2663148

Q1: Abstract: the number of patients included in the study belongs to material and method section, not to results.

Response:

Page 4, the 2nd paragraph: we move the sentence from “results” to “patients and methods”.

Q2: Core tip: please eliminate the sentence: Surveillance, however, is associated with concern, anxiety, and fear about the uncertainty of the diagnosis and the natural history of these cysts”. The following affirmation is not a direct conclusion from your study: Our findings may be helpful to stratify patients into those who require further cystic fluid testing and those who can be observed in a more lenient manner”.

Response:

We thank for reviewer’s comment and we revise the core tip as follows.

“Observation is advised for small pancreatic cyst without concerning features of malignancy. Our study explored that small pancreatic cysts with borderline pancreatic duct dilation, tubular shape, or septa were associated with risk of progression. Our findings may be helpful to stratify patients for different management planning according to their risk of progression”.

Q3: Material and method and results section: please specify the imaging methods used for comparison specifically in each group and for each time point. Also you should refer if there was any difference when different imaging methods were used

in the identification of the analyzed imaging features.

Response:

We thank for reviewer's comment and we revise it as follows.

- 1. The imaging modality for checking interval progression may be not the same one and is described in the page 8, Line 4-6: "The interval progression was examined by using the initial and the last imaging of cyst and may be not of the same imaging modality."*
- 2. MR imaging cannot detect calcification as CT scan does. Such interference caused by using different imaging modality to compare different group of patients is described in the page 11, the 3rd paragraph, the last 4 lines: "Calcification of pancreatic cysts was unable to be checked in 22 of our patients since they underwent MR imaging only. In the other 113 patients who had CT scan examined during the follow-up, only 4 patients had a calcified pancreatic cystic lesion and all calcification were located in the periphery."*