

Reviewer #1:

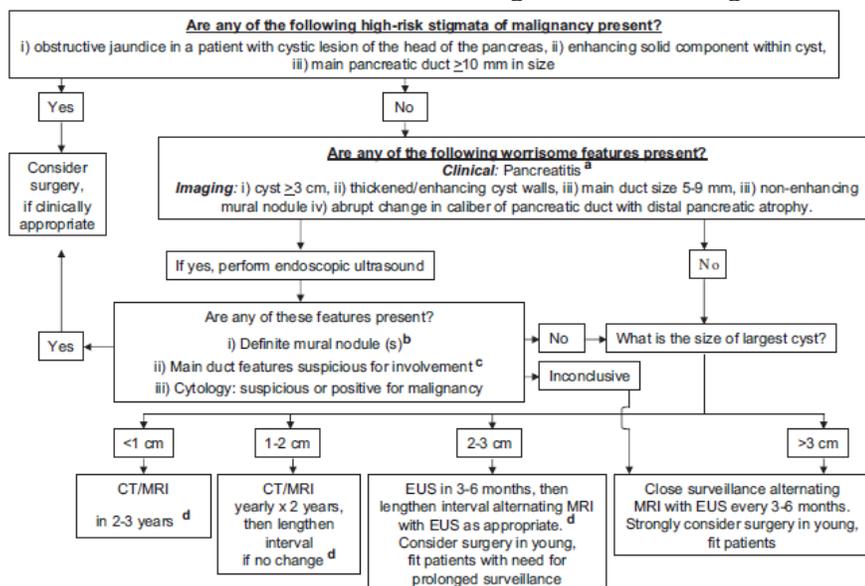
In their manuscript Khoi Nguyen et al investigated the "Effect of a Region-Wide Incorporation of an Algorithm Based on the 2012 International Consensus Guideline on the Practice Pattern for the Management of Pancreatic Cystic Neoplasms in an Integrated Health System". This study demonstrates the usefulness of the application of an algorithm in reducing the GI and surgeon visits and the use of EUS, thus reducing the cost for the health system. This study is well written and adds knowledge about the management of pancreatic cyst.

Response: Thank you for the positive comments.

Reviewer #2:

I read with great interest the manuscript entitled "Effect of a Region-Wide Incorporation of an Algorithm Based on the 2012 International Consensus Guideline on the Practice Pattern for the Management of Pancreatic Cystic Neoplasms in an Integrated Health System" by Andrew Khoi et al. Although the research is interesting the Authors should better discuss the advantages of the proposed algorithm. The Authors should simplify the explanation of their findings and the usefulness in the clinical practice. Additionally Figure 1 is too complex to be comprehended.

Response: We thank you for the comment and added a section in discussions that addresses advantages of the proposed algorithm and the simplified explanation of the usefulness in the clinical practice. We do acknowledge that figure 1 may be a bit too complex for an average clinician to comprehend. This algorithm was not created by the authors of this study but by the Kaiser Permanente leadership and is very similar to the Fukuoka version (please see below this response for the Fukuoka algorithm). The algorithm that the Kaiser leadership team came up with (figure 1 in the original manuscript) is used primarily by gastroenterologists (pancreatobiliary specialists in particular) and department leaders who need to know all the details; a simplified version of the recommendations depicted in table 2 is what is viewed by frontline physicians making clinical decisions after reviewing the reports of radiologic studies they ordered. In order to increase the practicality of such an algorithm, Kaiser Permanente added these simplified recommendations at the end of the reports of radiologic studies that detected PCNs. Regardless, in order to comply with reviewer #2, we took out the Kaiser Permanente algorithm from our revised manuscript and replaced it with the Fukuoka algorithm instead so that the readers would be able to see the original world-wide guidelines that Kaiser derived its version from.



a. Pancreatitis may be an indication for surgery for relief of symptoms.

b. Differential diagnosis includes mucin. Mucin can move with change in patient position, may be dislodged on cyst lavage and does not have Doppler flow. Features of true tumor nodule include lack of mobility, presence of Doppler flow and FNA of nodule showing tumor tissue

c. Presence of any one of thickened walls, intraductal mucin or mural nodules is suggestive of main duct involvement. In their absence main duct involvement is inconclusive.

d. Studies from Japan suggest that on follow-up of subjects with suspected BD-IPMN there is increased incidence of pancreatic ductal adenocarcinoma unrelated to malignant transformation of the BD-IPMN(s) being followed. However, it is unclear if imaging surveillance can detect early ductal adenocarcinoma, and, if so, at what interval surveillance imaging should be performed.

Reviewer #3:

It is difficult to predict the risk of malignancy, management of PCNs remains challenge. The short period of follow-up could not provide strong evidence for the algorithm. Furthermore, your study did not show how the algorithm improve patients' outcome.

Response: We appreciate this comment. We added the concern about the short follow-up period in the limitation section of discussions. The primary outcome of the study was not to examine the long-term natural course of PCNs but to evaluate the practice pattern change (i.e. EUS volume and GI/surgery consultations) months preceding and following the implementation of this world-wide algorithm. The aim of the study was not to show how the algorithm can improve patient outcome but to show the cost savings (without compromising patient care) that could result from the change in clinical practice after the dissemination of such an algorithm. We mention that we did follow the patients until May 1, 2017 (60 months from the beginning point of the study) to compare the rate of pancreatic malignancy between the two groups, which were not statistically significant. Therefore, although the study was not designed to show how the algorithm can improve long-term patient outcome, we conclude that the implementation of the algorithm did not result in worse patient outcome. A much longer study (perhaps following these PCN patients for over 5-10 years) would be needed to examine the true long-term outcome of not only the PCN algorithm but also the natural course of PCNs themselves.