For Reviewer #1.

Comments: Thses studies show that the symptoms of PC if present are not specific and there is a need for diagnosing preneoplastic lesion. Artificial inteligence (AI) models integrating multisource risk factors are the future of early PC diagnosis. The purpose of our study was to identify the current diagnostic methods for detecting PC by using noninvasive techniques with emphasis on early lesions and artificial inteligence. The article is novel and interesting. This publication impact clinical practice in the future. The authors need to draw a picture to describe the application of the current algorithm, and pointed the process of AI in the future. Besides, there are language problems in some places, which need to be improved.

Reply: Thank you for your comments. Our comments are as follows: We have added new illustrations (Figs.1-3) and we have revised the English language of the paper and sent it to a professional biomedical English language editing company.

For Reviewer #2.

Comments: The manuscript of Faur Alexandra Corina et al. provides a detailed overview of the current status of non-invasive methods for detecting PC, focusing on early lesions and AI. This is a very interesting aspect, considering the challenge on early detection of this disease in the general population. The overall English is adequate, even though I would suggest a review by the authors since there are some typos (for example ''typicaly'' instead of ''typically'' paragraph …). The abstract includes a background of the issue, concerns and suggestions but not a descriptive summary of the methods reported. The keywords do not reflect clearly the main focus of this manuscript and are repetitive. I would suggest to keep less of them and the most accurate. The introduction is well structured but I would suggest a deeper emphasis to the AI matter which is the main point of the manuscript. Methods are properly organized. I strongly recommend to homogeneously write all statistical data with numbers (Ninety percent of exocrine PC cases are pancreatic ductal adenocarcinoma (PDAC), with 80% ...) Legends of the table and figure must be added.

Reply: Thank you for your comments. Our comments are as follows: We have revised the English language using a professional biomedical English language editing

company, and we have also made the requested changes in the Abstract, Introduction and key words. Legends have been added as requested on the last page.

For Reviewer #3

Comments: This is a review focusing on the application of AI on the prediction and diagnosis of pancreatic cancer. Although the AI is a hotspot in the field of pan-cancers, the idea here is not innovative since there have been some similar reviews focusing on this issue. My concerns are as follows: 1.The description about the novelty of this article compared to other similar studies (e.g. Ref 1,2,4) is insufficient. In addition, the authors spent too much time on introducing the characteristics of PC and compositions of AI, which are not the crucial topics of this study. 2. There is a lack of information regarding the translational value of the results obtained by the studies mentioned in the manuscript. Are the results routinely applied in clinical practice or just reported in researches? 3. In Figure 1, 34 studies were included and 14 studies were excluded. Where are the remaining ones among the total studies reviewed? I was confused about the exact number of studies. 4. Then the author declared that "Twenty-nine eligible studies were included as follows 20 for current status in diagnostic methods in PC and 9 studies with implications in PC prediction by using AI algorithms." What is the exact number of studies involved, 34 or 29? 5. Although polished, the English language in the article is not entirely smooth regarding wording and grammar. e.g. the sentence "The authors aim to classify the IPMN as benign or malignant and the AI ability for predicting malignancy had an accuracy of 0.94, higher than the human preoperative diagnostic accuracy which was 0.56. This study had a number of limitations:it was retrospective, had a small sample of cases, with only internal validation and one center provided the cases" on page 13. 5. Please check the word "ofv" on page 6 , the word "eare"on page 14, the word "analized" on page 16,19 and the word "whit" on page 19. 6.On page 12,the sentence"87-91 specificity and 80% specificity" is probably not what the authors intended to write. 7.On page 13, the sentence "The authors aim to classify the IPMN as benign or malignant and the AI ability for predicting malignancy had an accuracy of 0.94, higher than the human preoperative diagnostic accuracy which was 0.56" should be modified. 8. What does it mean by the sentence "AI methods can represent the needed step to reach a standardized interpretation of patient data and

investigations whilereducing human bias or error" on page 18. 9. On page 18, the sentence "A collaboration between governments, scientists and academic centers such as was seen in the COVID-19 era proves that humans from different countries and continents can work together in sharing information in a common attempt to save lives and stop the virus. Their collaborations proved the existing potential of scientists working together to create creating a vast database" should be modified. 10. The limited references are insufficient to summarize the conclusions. Besides, please check the styles of all the references according to the World Journal of Gastroenterology guidelines.

Reply: Thank you for your comments. Our comments are as follows:

Comment No 1: We agree with you that the application of AI in cancers prediction of is not an innovative idea hence we focused specifically on pancreatic cancers. We note that despite the publication of articles focusing on the diagnosis of pancreatic cancer with the aid of AI only a small amount of research has focused on early lesions and methods of prediction. We started our search by focusing on finding articles that described the development of algorithms for detecting early lesions in pancreatic cancer and we found only a small number of such articles, hence we became interested in investigating this subject futher. We broadly presented the current knowledge on this subject because it sets the context in which AI can be used. The current status of pancreatic cancer diagnosis in terms of all the tests and the lesions that can be futher evaluated with AI must be presented in our opinion as an introduction and the methods of analysis also for a better understanding of the concept of how and where AI can be used to predict or diagnose early pancreatic cancer. We have worked to futher summarize the initial text and emphasize all the data that can be obtained by using artificial intelligence algorithms. Additionally we have tried to preserve our initial ideea - we have to present all the data and the methods of AI that can be used to analyze the factors and correlate the obtained information in order to achieve a machine-assisted diagnosis that can be used in hospitals in the future.

Comment No 2: Yes, there is a lack of information offered by the studies that we found and analysed and all of those aspects have been emphasized in the text by reporting their limitations. At this time there are only a small number of studies that focused on

the subject of early lesions of pancreatic cancer so the results have to be further validated in order to become more widespread and routinely used. We have summarized the aspects of validation in the table with an additional column indicating that all studies were retrospective.

Coments No 3 and 4: We included 34 references because there are two datasets one focusing on methods of diagnosing pancreatic cancer and early lesions and the other on reports that anayzed early lesions with AI methods. For the second dataset 29 studies were included and we chose only 9 for our analyses because in our opinion these studies focused mainly on prediction and early lesion with the help of AI algorithms and were not reviews. We hope that now we have made this more clearer; we have revised the text, added new references, identified a new study and added the results to our manuscript, made new figures and updated the table.

Comment No 5: As requested for the language editing section, we have sent the document to a professional biomedical English language editing company who have provided a cetificate for their language editing. We revised the sentences and sent again the document to the company to polish the language again.

Coments No 6 and 7 comment: We have corrected the issue you raised.

Comment No 8: We have corrected the grammar issue. Additionally we felt that the rest of the sentence sumarised our conclusion after reading a large number of articles published about artificial inteligence in medicine. There are differences between machine learners and humans. An analysis made by humans is subjected to bias resulting from a series of factors, including the: level of expertise and, how a specific doctor thinks and correlates the knowledge learned about a disease and the data of a patient, hence the different first and second opinions about a diagnosis between healthcare professionals. Some of those opinions could also be sources of errors in diagnosis. In machine learning we think that if we know beforehand the method of diagnosis about a specific disease for which an AI algorithm was trained, the output should be the same at any one moment in time, which reduces the possibility of a diagnosis depending on human factors. Despite the time and costs needed to train a computer model the future medicine lies in AI, at least for the first steps of diagnosis

in identifying patients before reaching the specialization that has to deal with his or her specific disease.

Comment No 9: We have revised the original ideea but we still consider that COVID-19 has truly united the world like never before in a time in which advanced computer tools are available to help in the fight against diseases. We have experienced wars but now we also have a techique that can help. Why not add a phrase in a scientific paper to emphasize that it is possible to work together, to create a network of knowledge for medical purposes?. We ask you to accept this ideea because we think that the basis of international collaboration was established with the Covid-19 pandemic.

Comment No 10: The list of references is limited by the subject that we have chosen, nevertheless, we sought to identify additional studies. We have added new references and we have checked the style to match the requirements of the journal accordingly.