Dear Editors and Reviewers:

Thank you for your letter and the reviewers' comments concerning our manuscript entitled **"A personal predictive model based on systemic inflammation markers for estimation of postoperative pancreatic fistula following pancreaticoduodenectomy" (Manuscript NO: 77502).** These comments have important guiding significance for our research. We have carefully studied the comments and corrected them in the hope of approval. The modified part is marked in red on the paper. The main corrections in the paper and the responses to the comments of editors and commentators are as follows:

Responses to the Reviewer 1 comments:

Reviewer #1: interesting approach to the topic of pancreatic fistula, which is a subject that has been much explored in the literature and still has a lot to learn; surely any attempt to mitigate the problem will always be welcome. Great writing, I suggest using the acronym POPF for pancreatic fistula and PD for pancreaticoduodenectomy.

Authors response: Thank you for your suggestion. We also agree with you that using the acronym POPF for pancreatic fistula and PD for pancreaticoduodenectomy. We have revised and corrected the text according to your suggestions. As follows: Postoperative pancreatic fistula (POPF) is a serious life-threatening complication following pancreatoduodenectomy (PD).

Responses to the Reviewer 2 comments:

Reviewer #2: The article is within the scope of the journal, and deals with an interesting topic. It is well written and structured. It is smooth to read. The experiment described is well designed. The results are displayed and discussed. The contribution of the article represents an advance in the area of knowledge. However, I suggest the following two improvements: a) The state of the art of the problem dealt with should be expanded in the introduction. b) The conclusions should be improved by synthetically indicating what the scientific contribution is and proposing a set of lines of work.

Authors response: Thank you for your suggestion. We highly agree with the following suggestions you put forward, and we have made corresponding changes according to your suggestions, as follows:

a) The state of the art of the problem dealt with should be expanded in the introduction.

Response: In order to highlight the innovation of this study, we added the following contents in the preface, as follows:

At present, a series of serum markers provide evidence that detecting systemic inflammation may be associated with the risk of benign and malignant disease progression. Meanwhile, the systemic response to postoperative local inflammatory stimulation is closely related to the complications after gastrointestinal surgery. Traditionally, finding the best value for these free parameters is an arduous task. Fortunately, the machine learning algorithm represents a computational method for effectively navigating the free parameter space to obtain a good model. In addition, machine-learning(ML) has been widely used in medical science. These unceasing new algorithms and iterative analyses might be useful for prognostication in cases and optimize individual treatment decisions. Collectively, a high-performing model requires multiple attributes for success, the combination of characteristic variables has facilitated to elevate predictive performance while minimizing the prediction error.

b) The conclusions should be improved by synthetically indicating what the scientific contribution

is and proposing a set of lines of work.

Response: We agree with your suggestion that “The conclusions should be improved by synthetically indicating what the scientific contribution is and proposing a set of lines of work.” In this study, we have revised the conclusion as follows:

In the abstract part: Conclusion

In conclusion, in-depth learning based on fluctuating serological inflammatory markers can be used as a powerful and promising tool to guide optimal treatment, clinical management and prevent or mitigate adverse consequences. In the future, the most clinically relevant endpoint should be used to prospectively verify the prognostic and predictive utility of molecular classification schemes.

In the “conclusion” part:

Collectively, our findings provide insights into the candidate predictive markers(HALP, NAR, CRP, PCT, and PLR) associated with a high risk of POPF via serum inflammatory secretion, how they can be manipulated to develop ML-based predictive models, and the prediction performance of these unsupervised ensemble models might be at a population-based level. In the future, we anticipate that these findings will extend external studies seeking to strengthen valuable adjunct information and guide treatment decisions.

Responses to the Editorial Office's comments:

1) Science Editor: 1)The theme of the manuscript fall within the scope of the journal,2)no academic misconduct was found, 3) the manuscript provide insights into the candidate predictive markers(HALP, NAR, CRP, PCT, and PLR) associated with a high risk of post-operative PF via serum inflammatory secretionthe, 4) The langue was edited by Charleworth, 5) Minor revision.

Language Quality: Grade B (Minor language polishing)

Scientific Quality: Grade C (Good)

Authors response: Thank you for your suggestion. we have submitted to our paper, the Charlesworth Author Services (CAS) team (https://www.cwauthors.com.cn/) had helped us improve our language and correct grammatical errors existed in our manuscript. The CAS team confirmed that their proofreader had done a very good job of improving language and correcting grammatical errors. We also checked the manuscript again and again, and we couldn’t find grammatical errors.

2) Company Editor-in-Chief: I recommend the manuscript to be published in the World Journal of Gastrointestinal Surgery. Before its final acceptance, the author(s) must provide the Signed Informed Consent Form(s) or Document(s). For example, authors from China should upload the Chinese version of the document, authors from Italy should upload the Italian version of the document, authors from Germany should upload the Deutsch version of the document, and authors from the United States and the United Kingdom should upload the English version of the document, etc.

Authors response: Thank you for your suggestion. We have reorganized and provided the uploaded and signed informed consent form or documents(Chinese version of the document) according to your requirements.

We tried our best to improve the manuscript and made some changes in the manuscript. These changes will not influence the content and framework of the paper. We appreciate for

Editors/Reviewers' warm work earnestly, and hope that the correction will meet with approval. Once again, thank you very much for your comments and suggestions.