Author’s response to reviews

Title: Serum D-dimer Levels at Admission for Prediction of Outcomes in Acute Pancreatitis

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Editor Comments:

Please consider the following changes
1) Change of title to "Serum D-dimer Levels at admission for Prediction of outcomes in Acute Pancreatitis"
   Respond: We couldn't agree with you more. We will change the title to "Serum D-dimer Levels at admission for Prediction of outcomes in Acute Pancreatitis". (e.g. Title section, line 1, page 1)
2) Conclusion part in abstract be changed to "The measurement of D-dimer levels at admission may be useful in the risk stratification of AP."
   Respond: Thank you. We will change the Conclusion part in abstract to "The measurement of D-dimer levels at admission may be useful in the risk stratification of AP." (e.g. Abstract section, line 39, page 1)
3) The use of English is still awkward at many places
   Respond: Thank you. The manuscript has been modified by the professional English editing (American Journal Experts).
4) How was the cutoff of 2.5 arrived at?
Respond: Thank you. We choose the day 1 of D-dimer levels to make the AUROC curve and calculate the optimum cut-off.

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Reviewer reports:
WQ Li (Reviewer 1): Early prediction of acute pancreatitis (AP) severity is one of clinical work and research focus. Although many studies and various prediction methods have been reported, there is still a long way to go from clinical application. This is a good study. First, the sample size is large, and time stratification is carried out according to the different time after admission. Second, D-dimer is a test index which has been routinely used in clinical practice to facilitate the later clinical application. Although there are some articles on D-dimer and AP (including those of our team), I still think this is a good clinical study and worth publishing. Of course, there are some problems in the article, which need to be revised.

1. Please utilise the assistance of a Professional English Language editing service - the manuscript is ridden with language errors throughout, which distracts readers from the message the authors wish to get across.
Respond: Thank you. As we mention above, this manuscript has been modified by the professional English editing (American Journal Experts).

2. There are several abbreviations used throughout the manuscript without clarifying to the reader what they actually mean. One must not assume that the abbreviations used are universally accepted, even among pancreatologists. Will the authors please ensure that these are clarified throughout the manuscript?
Respond: Yes, I am sure. All of the abbreviations have been clarified in the end of the manuscript and the abbreviations are widely used by researchers and clinicians. (e.g. Declarations section, line 23, page 2)

3. Also, if the submitted manuscript is to be revised, I would strongly advise the authors to review all their data on AP and strictly classify the severity of AP in their patients as suggested by the landmark paper by Banks et al.
Respond: Thank you for your valuable advises, we reviewed all of data in patients and strictly classified the severity of AP as suggested by Banks et al. (e.g. Methods section, line 8, page 6)

4. In the discussion section, please explain the possible mechanism of D-dimer caused aggravation of pancreatitis
Respond: OK, we'll discuss the possible mechanisms in detail in the discussion. (e.g. Discussion section, line 11, page 5)

5. Some percentages in the chart are suggested to be replaced by One decimal post-point.
Respond: OK, we will change it. Thank you.

6. This study is a retrospective study, and a prospective large samples study should be designed to verify this conclusion in the future.
Respond: We plan to design a prospective trial to predict patient outcomes and interventions in the future. Thank you.

K Sun (Reviewer 2): Please include all comments for the authors in this box rather than uploading your
This clinical research work by Drs. Wan et al., investigated the effects of serum D-dimer level as an indicator for the early prediction of acute pancreatitis (AP) outcome upon admission. They analyzed 3451 clinical patients for their D-dimer level and their correlation with various stages of acute pancreatitis. The authors concluded that measurement of D-dimer levels may be useful in the early risk stratification of AP and prediction of prognosis, because this is an important clinical topic, this work is therefore interesting with merit. The manuscript is generally well written but with many grammatical typos, and appears in its early version of submission, due mostly to some of the statements need to be amended and revision. Authors are encouraged to revise and make the manuscript logically sound and more attractive.

Minor points:
1. There are some minor typos in the text and one sentence in the result part is only half finished, which deserve correction.
   Respond: OK, we will correct them. Thank you.
2. Two major markers for pancreatitis are serum lipase and amylase, which were not mentioned or missing and were not analyzed in the study, it is not clear the rational why they were omitted for such tedious and important study, please explain and discuss.
   Respond: Although amylase and lipase are an indispensable indicator in the diagnosis of pancreatitis, they are also proved to be not proportional to the severity of the disease. (Lankisch PG, Apte M, Banks PA. Acute pancreatitis. Lancet. 2015;386(9988):85–96) Because they tend to be low in some patients with severe acute pancreatitis.
3. There are mistakes in the reference part, such as ref. #10, which require correction, and the format appears different among references which deserve author's attention.
   Respond: well, we will correct the reference and keep them consistent. Thank you.
4. The overall quality of the work could be improved by adding more data, such as serum lipase and amylase, and in-depth analysis of these data between subgroups.
   Respond: We are sorry that we can't agree this opinion. Because this paper focuses on d-dimer as an independent predictor of severe acute pancreatitis, amylase and lipase have been shown in some study that their levels are not correlated with severity. (Lankisch P G, Burchard-Reckert S, Lehnick D. Underestimation of acute pancreatitis: patients with only a small increase in amylase/lipase levels can also have or develop severe acute pancreatitis [J]. Gut, 1999, 44(4): 542-544.) It has been noted that serum amylase concentrations may be normal in alcohol-induced AP and hypertriglyceridemia. (Yadav D, Agarwal N, Pitchumoni C S. A critical evaluation of laboratory tests in acute pancreatitis [J]. The American journal of gastroenterology, 2002, 97(6): 1309.) Therefore, we don't think it is necessary to analyze the relationship between amylase and lipase and the severity of pancreatitis.