Author's response to reviews

Title: Significance of serum procalcitonin as biomarker for detection of bacterial peritonitis: A systematic review and meta-analysis

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Author's response to reviews:

Dear Dr Nathaniel Nazareno,

We respectfully send back our manuscript: Significance of serum procalcitonin as biomarker for detection of bacterial peritonitis: A systematic review and meta-analysis (Manuscript-ID: 1214158141168816) for the consideration of publication in Journal of BMC infectious diseases.

We greatly appreciate the efforts of the reviewers for the valuable and constructive comments on previous draft. Based on their comments and requests, we have carefully taken their comments into consideration and made extensive modification on the original manuscript. The following summarizes how we responded to reviewer comments. A revised manuscript with the correction sections marked was attached as the supplemental material and for the purpose of easy check.

Here is our response to their comments.

Revision — authors’ response

Reviewer #1

Major Compulsory Revisions

Comment-1: The introduction should include some epidemiological data about the prevalence of bacterial peritonitis in adult patients. The first paragraph should be shortened.

Response: Thanks for your valuable comments on our paper. We have added the text of describing the epidemiological data about the prevalence of bacterial peritonitis “Previous studies showed an average peritonitis...” in the first
paragraph of the chapter of “INTRODUCTION”, and added related references. In addition, some sentence in the first paragraph has been deleted, please check it.

*Added related references:


Comment-2: Results, study characteristics, first paragraph, line 1 to 3, and Table 1: The systematic review included 2 studies from the same investigators’ group: Zhang W et al. (Chin J Infect Dis 2003) (ref. 24), and Zhang W et al. (Chin J Clin Hepatol 2004) (ref. 27). The serum PCR cut-off value used in both studies was different. Did the authors check that the patients recruited in these two studies were from different cohorts? If so, this point should be stated. If the cohort of patients was the same in both studies, the data with the highest Youden index should be used for the meta-analysis, as mentioned in Materials and methods for the results reported at different cut-off values in a same study.

Response: Thanks for your valuable comments on our paper. We have carefully checked the included studies, and found that the 89 patients in Zhang W et al. (Chin J Infect Dis 2003) were recruited from March 1997 to November 2000 in Chinese 302 People’s Liberation Army Hospital, while the 62 patients Zhang W et al. (Chin J Clin Hepatol 2004) were recruited from March 2000 to August 2001 in Chinese 302 People’s Liberation Army Hospital, so these patients were recruited from different cohorts, and we have added a sentence “There were two trials performed by the same research unit, but the patients in these two studies were recruited from different cohorts“ in the chapter of Study Characteristics. Please check it.

In addition, We have checked the search strategy on MEDLINE, EMBASE, SCOPUS, Cochrane databases, China Biology Medicine Database(CBM), and China National Knowledge Infrastructure Database(CNKI) (all to April 2014), and added four new trials. We have carefully checked all the included studies and found there are some errors in the included data due to our carelessness, in the trial performed by Guz et. al. (reference 17), sixteen PD patients had 21 episodes of PD peritonitis during the study period, and the number of control group is 35. Regarding the study by Lam 2008, 35 PD patients had peritonitis out of 200, while 0.38 ng/ml was the cut off that best predicted micro-inflammation at 42 days for patients diagnosed with peritonitis but not a cut off derived for diagnosing peritonitis. We have incorrectly used the PCT cut off of 0.38 ng/ml for diagnosing peritonitis to our carelessness, while the correct sensitivity of diagnosis for peritonitis was 80%(28/35) when using PCT >0.5 ng/mL as the cutoff, and we have written to the corresponding author of that paper (Dr. Lai KN, Email: klnai@hkucc.hku.hk) for the specificity of diagnosis for peritonitis (92%). We have modified these errors in the new Table 1. In addition, the study flow diagram has been modified. Please check it, thanks a lot.
*Added related references:


Comment-3: Results, study characteristics, first paragraph, line 5 to 8, and Table 1: The authors claimed that 8 studies referred to cirrhotic patients and 2 studies (ref. 22 and ref. 23) were performed in patients with chronic severe hepatitis. Actually, Connert et al. (ref. 23) included patients with cirrhosis in their study. Therefore, 9 studies with cirrhotic patients, and 1 study with chronic severe hepatitis patients should be mentioned in the results section and in table 1. The respective references should be corrected in accordance with these changes.

Response: Thanks for your valuable comments on our paper. We have added four new trials after researched from multiple databases. And there were 4 studies were of peritonitis in peritoneal dialysis patients[17-20], 12 studies were of spontaneous bacterial peritonitis in cirrhotic patients[21-23, 25-32, 34], 1 studies were from spontaneous bacterial peritonitis of chronic severe hepatitis patients[24], and 1 study was from spontaneous bacterial peritonitis of end stage liver disease patients[33].

Regarding the trial performed by Connert et al, we have reclassified this study from chronic severe hepatitis patients group to cirrhotic patients group both in the results section and in table 1. Please check it, thanks.

Comment-4: Results, subgroup analysis, first paragraph, line 4 to 8, and Table 2: The subgroup analysis reported 4 studies that used a PCT cut-off value of less than 0.5 ng/mL (ref. 16, 19, 21, 22). However, the low cut-off value (0.3 ng/mL) used in the study of Viallon et al. (ref. 21) referred to ascitic PCT and not serum PCT. Therefore, the subgroup analysis of serum PCT with a cut-off value < 0.5 ng/mL should include only 3 studies (ref. 16,19, 21). The range in this subgroup is 0.38-0.48 ng/mL (see also table 2).

Considering the small size of the 2 subgroups with lower serum PCT cut-off
values, and the narrow discriminating range between them (4 studies: 0.5 ng/mL, and 3 studies: 0.38-0.48 ng/mL), these 2 categories should be merged in a larger single subgroup named “low cut-off value” (7 studies: less or equal to 0.5 ng/mL). The respective pooled sensitivity, specificity, DOR, AUROC, positive and negative likelihood ratios, should be determined again. The comparison with the “high cut-off value” subgroup will be more reliable, without changing the main conclusions of the results.

Response: Thanks for your valuable comments on our paper. We have added four new trials after researched from multiple databases, and we have re-performed subgroup analysis stratified by PCT cut-off value, there are 9 studies that used a PCT cut-off value of more than 0.5 ng/mL, 9 studies that used a PCT cut-off value of equal to 0.5 ng/mL, and 3 studies that used a PCT cut-off value of less than 0.5 ng/mL, we have modified relevant contents in the chapter of Subgroup analysis and Table 2, please check it, thanks.

In addition, we have added the functional assay sensitivities (FAS) of different PCT assays in the Table 1 to clarify difference more clearly, and the subgroup analyses based on the PCT assays with the same FAS was performed.

Comment-5: Discussion, 4th paragraph:
The issue about the potential production of PCT in the ascitic fluid is interesting. However, the conclusion that the accuracy of ascitic PCT for the diagnosis of bacterial peritonitis could be better than serum PCT is not convincing. Results found in the ascitic PCT subgroup were compared with those of overall serum PCT analysis.
The total number of patients included in subgroups should be reported. Actually, there is an overlap between the 95% confidence intervals (CI) in each group, so that the difference was not significant. Nevertheless, as ascitic PCT was determined in cirrhotic patients only, the comparison of results should be drawn with those of serum PCT in cirrhotic patients’ subgroup. In that case, the difference in AUROC (0.94 [95% CI 0.91-0.95], versus 0.87 [95% CI, 0.84-0.90], respectively) may suggest a better diagnostic accuracy of ascitic PCT. However, the PCT sensitivity, specificity, and DOR were similar in both subgroups. These small and in part not significant differences rather support the assumption of Viallon et al. (ref. 21) that PCT detection in the ascitic fluid was the result of a passive shift due to increased vascular permeability instead of an intraperitoneal synthesis.

Response: Thanks for your valuable comments on our paper. We have added four new trials after researched from multiple databases, and there is one more trial performed by Xie et al (Ref.34 ) reporting accuracy parameters on ascitic
PCT. We have modified relevant content in the third paragraph of the chapter of Diagnostic accuracy indices. In addition, some sentences in third paragraph of the chapter of DISCUSSION has been modified. Please check it.

Comment-6: Discussion, 6th paragraph, line 7 to 8:
The different analytical methods used to determine PCT may contribute to the heterogeneity between studies to some extent. Actually, only two different methods were used for the measurement of PCT: a quantitative immunoluminometric assay, including the LUMItest, and a semi-quantitative immunochromatographic assay, the PCT-Q test.

Response: Thanks for your valuable comments on our paper. As all these included studies using different PCT assays with widely varying functional assay sensitivities (FAS), we have added the FAS of different PCT assays in the Table 1 to clarify difference more clearly. In addition, the subgroup analyses based on the PCT assays with the same FAS was performed, but the result showed that there was no difference on the diagnostic value of PCT among trials of different PCT assays (DOR, 65.43; AUROC, 0.95 vs DOR, 71.41; AUROC, 0.95; shown in Table 2). In addition, we have added this subgroup analysis result in the chapter of “Subgroup analysis” please check it, thanks a lot.

Comment-7: Discussion, 7th paragraph, fourth limitation, last sentence, line 12 to 14: A publication bias is a potential limitation of the present systematic review. Although an extensive database search was performed, it is possible that the analysis included the results from published studies with positive findings. This issue should be addressed by drawing a funnel plot, and the results reported as appropriate.

Response: Thanks for your valuable comments on our paper, we have tested the possible publication bias using Deek’s test, the analysis showed that there was no significant evidence of potential publication bias, and the results has been added in the new Table 2.

We have added some sentences: "To test for possible publication bias, we constructed effective sample size funnel plots versus the log diagnostic odds ratio and did a regression test of asymmetry (Deek’s test)…". in the chapter of “MATERIALS AND METHODS, Data synthesis and statistical analysis”. In addition, a chapter of: "Publication bias" has been added at the end of “Results”

Regarding the fourth limitation in the chapter of Discussion, we have modified it to: "Fourth, despite no significant publication bias was detected, however, this study included 8 low-quality Chinese language trials, which may lead to an overestimation of overall diagnostic accuracy of PCT, especially because positive studies are more easily reported", please check it.

Comment-8: Discussion, 7th paragraph, limitations:
The fact that the study was restricted to English and Chinese language should be
stated as an additional limitation. This point could be mentioned as the fourth limitation, before the issue of a potential publication bias.

Response: Thanks for your valuable comments on our paper, we have modified the sentence to: "Fourthly, this study was restricted to English and Chinese language trials, despite…..”, please check it. In addition, we have performed the subgroup analyses based on different countries and different human race, the result showed that the value of serum PCT to diagnosis peritonitis in trials published in Chinese (DOR,141.09; AUROC,0.92) was substantially higher compared with that published in English (DOR,29.16; AUROC, 0.92; shown in Table 2).

Comment-9: Table 1 and Table 2:
The total number of patients included in each study (Table 1) and subgroup (Table 2) should be added in the tables

Response: Thanks for your valuable suggestions, we have deleted the column of “prevalence (N) in Table 1, and the Table 1 has been re-written, the columns of “Design, Case/Control, TP, FP, FN, TN,” and the FAS of different PCT testing systems were added in the new Table 1. In addition, we have added a column of total number of patients in the Table 2, please check it.

Reviewer #2
Major Compulsory Revisions

Comment-1: Comparative data about procalcitonin significance in fungal peritonitis must be added. The authors should describe how the aetiology of peritonitis is linked with the procalcitonin level and if not, how the discrimination between bacterial and fungal peritonitis can be done. Fungal peritonitis are quite uncommon, but can occur in peritoneal dialysed patients.

Response: Thanks for your valuable suggestions, we have researched the studies about procalcitonin significance in fungal peritonitis from multiple databases, however, there is no relevant trials. On the other hand, we have added some sentence in the fifth paragraph of the chapter of DISCUSSION:” Fungal peritonitis is a quite uncommon but potentially fatal complication both in peritoneal dialysed and advanced liver cirrhosis patients……

*Added related references:


Comment-2: Title is not very clearly formulated ("Significance of serum
procalcitonin as biomarker for detection of bacterial peritonitis” could be use instead).

Response: Thanks for your valuable suggestions, the title has been modified to;” Significance of serum procalcitonin as biomarker for detection of bacterial peritonitis: A systematic review and meta-analysis”.

Comment-3: According to Spahr et al. (2001), "Procalcitonin is not an accurate marker of spontaneous bacterial peritonitis in patients with cirrhosis" - Hepatogastroenterology, 48(38):502-505. Is this compatible with their conclusion?

Response: Thanks for your valuable comments on our paper, there is a significant body of clinical research indicates good diagnostic accuracy for the PCT test for discrimination bacterial infection. However, the overall diagnostic value of PCT remains unclear, and there are controversial whether PCT test is beneficial, such as the trial performed by Spahr et al. (Ref.22) showed that PCT is not an accurate marker of spontaneous bacterial peritonitis in patients with cirrhosis. But our pooled analysis of 18 trials show that PCT determination is a relatively sensitive and specific test for the diagnosis of bacterial peritonitis, in line with our finding, the systematic review included the trial performed by Spahr et al also suggest moderate to high accuracy for PCT as a diagnostic aid for spontaneous bacterial peritonitis.

Minor Essential Revisions
Reviewer #1
Comment-1: Abstract, methods:
The name of databases used for the systematic review should be mentioned in the abstract. The STATA 12.0 software should not be mentioned in the abstract.
Response: Thanks for your valuable comments on our paper, relevant sentences in the ABSTRACT has been modified to: “We performed a systematic searched from MEDLINE, EMBASE, SCOPUS, China Biology Medicine Database(CBM), and China National Knowledge Infrastructure Database(CNKI) and Cochrane databases…”, and we have deleted the words:” by Stata 12.0 software” please check it.

Comment-2: Abstract, results:
The total number of patients included (n=1179) should be stated in the abstract.
Response: Thanks for your valuable comments on our paper, the first sentence in the Abstract, Results has been modified to: "Eighteen studies involving 1827 patients were included for the present meta-analysis…”, please check it.

Comment-3: Introduction, second paragraph:
The first sentence is in part duplicated from Wacker et al. (ref. 5), and should be modified.
Response: Thanks for your valuable comments on our paper, we have modified this sentence to: “Several potential biomarkers have been proposed in highly cited studies for their ability to diagnose bacterial infection, procalcitonin (PCT), which is a precursor of calcitonin including 116-aminoacid polypeptide had been indicated the “the champion” so far....” In addition, the study performed by Wacker et al has been cited (ref. 4).

Comment-4: Materials and methods, data synthesis and statistical analysis, line 10-11:
The value of I2 statistic > 50 % means a moderate to high heterogeneity. It is better not to use the term “significant”, since even a low heterogeneity may be statistically significant.
Response: Thanks for your valuable comments, we have modified the word: “significant” to “a moderate to high”, please check it.

Comment-5: Results, data extraction and calculation, last sentence:
The range of cut-off values for serum PCT should be corrected: it ranged from 0.38 to 13.7 ng/ml.
Response: Thanks for your valuable comments, in the study performed by Lam 2008, 35 PD patients had peritonitis out of 200. while 0.38 ng/ml was the cut off that best predicted micro-inflammation at 42 days for patients diagnosed with peritonitis but not a cut off derived for diagnosing peritonitis. We have incorrectly used the PCT cut off of 0.38 ng/ml for diagnosing peritonitis to our carelessness, while the correct sensitivity of diagnosis for peritonitis was 80%(28/35) when using PCT >0.5 ng/mL as the cutoff, so we have modified the words to: “0.42-13.7ng/ml”, please check it.

Comment-6: Results, diagnostic accuracy indices: The first sentence could be deleted, and the reference to figures 5 and 6 should be added in the following text, as appropriate. The polled sensitivity and specificity should be reported before the results of ROC and AUROC. Similarly, the reference to figures 5 and 6 should not precede the reference to figures 3 and 4.
Response: Thanks for your valuable comments, relevant contents has been modified in the chapter of Diagnostic accuracy indices, please check it.

Comment-7: Results, PCT and long-term adverse outcomes of peritonitis: The last sentence about the need for more prospective research should be deleted from the results section. This issue is already addressed in the discussion.
Response: Thanks for your valuable comments, the sentence:” More prospective research is needed to elucidate the definite evaluating prognostic abilities of PCT in peritonitis patients” has been deleted, please check it.
Comment-8: Conclusion, line 5-8:
The sentence is in part duplicated from Wacker et al. (ref. 5), and should be modified or the reference should be cited.
A modification could be as follows: “However, it is important to note that PCT cannot be recommended as a “gold standard” test for peritonitis up to now, and should be interpreted in combination with other clinical, analytical, and/or microbiological data. Given the limits of PCT as a single marker, additional large prospective studies should determine its diagnostic value in bacterial peritonitis, when interpreted in association with other biomarkers”.
Response: Thanks for your valuable suggestions, These sentence has been modified to: “However, it is important to note that PCT cannot be recommended as a “gold standard” test for peritonitis up to now, and should be interpreted in combination with other clinical……”, please check it.

Comment-9: References:
[18]: Turk J Med Sci
Response: Thanks for your valuable suggestions, we have checked the References 20: “Assessment of procalcitonin and other inflammatory markers in peritoneal dialysis-related peritonitis” on SCOPUS, the journal of this paper is “Turk J Med Sci”, and we have already modified the journal name to: “Turk J Med Sci”, please check it.

Comment-10: Table 1:
The column “Outcomes definition” should be positioned before column “Prevalence”. The column “Cut-off” should be positioned close to column “Sensitivity, specificity”, so that the respective values are adjacent, and the 15 footnotes may be deleted.
Response: Thanks for your valuable suggestions, we have modified relevant contents in the new Table 1, we have deleted the column of “prevalence (N) in Table.1, and the Table 1 has been re-written, the columns of “Design, Case/Control, TP, FP, FN, TN,” and the FAS of different PCT testing systems were added on the new Table 1, please check it.

Reviewer #2
Comment-1: The words spelling must be revised (e.g. "ascitic", not "ascetic" etc.).
Response: Thanks for the kind and gracious comments, there is some spelling mistakes in the draft manuscript, We have checked the whole article carefully to improve the English writing, corrected typing errors, and the term: “ascetic” has been replaced with “ascitic”, please check it, thanks.
Comment-2: Use abbreviations only after the word was first full-typed in the text.
Response: Thanks for the kind and gracious comments, we have added some full-typed words before abbreviations in the manuscript.

Discretionary Revisions
Reviewer #1
Comment-1: Running title:
“Procalcitonin in bacterial peritonitis”.
Response: Thanks for the kind and gracious comments, we have modified the running title to: “Procalcitonin in bacterial peritonitis”.

Comment-2: Introduction, first paragraph:
The micro-organisms cited should be “Gram negative bacilli”.
Response: Thanks for the kind and gracious comments, the terms: “Escherichia coli” has been replaced with: “Gram negative bacilli”.

Comment-3: Materials and methods, data extraction and quality assessment, last sentence: The reference to Stata 12.0 software should be given only once, preferably in the next paragraph.
Response: Thanks for the kind and gracious comments, we have modified these contents, please check it.

Comment-4: Results, quality assessment, line 5-9:
The definitions of peritonitis were already detailed in the study characteristics and should not be repeated in this section.
Response: Thanks for the kind and gracious comments, we have deleted the definitions of peritonitis in the chapter of Quality Assessment, and added a sentence: “however, as different definitions were used in different trials” at line 6 in the chapter of Quality Assessment, please check it.

Comment-5: Discussion, 3rd paragraph, line 4:
The sentence “PCT is a well-known acute-phase reactant protein” should be deleted.
Response: Thanks for the kind and gracious comments, we have deleted this sentence.

Minor issues not for publication
Reviewer #1
Spelling
Comments
1. Introduction, second paragraph: “[...] produced by extrathyroidal cells (e.g.}
monocytes).
Response: Thanks for your valuable suggestions, we have modified the word: “extrathyroid” to “extrathyroidal”.

2. Materials and methods, data sources and search strategy, line 8: “Figure 1 shows details of the search […]”.  
Response: Thanks for your valuable suggestions, we have modified the word: “showed” to “shows”.

3. Materials and methods, data extraction and quality assessment, line 6: “[…], and in case of missing data, […]”.  
Response: Thanks for your valuable suggestions, we have added a word: “and” before the sentence: “in case of missing data…”.

4. Materials and methods, data synthesis and statistical analysis, line 10: “[…] cut-off points”.  
Response: Thanks for your valuable suggestions, we have modified the word: “cutoff” to “cut-off”.

5. Results, identification of studies, first sentence: “Overall, our electronic search […]”.  
Response: Thanks for your valuable suggestions, we have modified the words: “in all” to “overall”.

6. Results, data extraction and calculation, line 4-5: “cut-off values”.  
Response: Thanks for your valuable suggestions, we have modified the word: “cutoff” to “cut-off”.

7. Results, subgroup analysis, first paragraph, last sentence: “cut-off values”.  
Response: Thanks for your valuable suggestions, we have modified the word: “cutoff” to “cut-off”.

8. Results, PCT and long-term adverse outcomes of peritonitis, line 8: “[…] patients who died or survived during the follow-up period […].”  
Response: Thanks for your valuable suggestions, we have modified the word: “follow up” to “follow-up”.

9. Discussion, 1st paragraph, line 13-14: “[…] detection and differential diagnosis of inflammatory states […]. However, there are few meta-analyses on the accuracy of PCT […].”  
Response: Thanks for your valuable suggestions, we have modified the word: “diagnostics, analysis” to “diagnosis, analyses”.

10. Discussion, 4th paragraph, line 5 and 7: “ascitic PCT […]” and “ascitic fluid”.
Response: Thanks for your valuable suggestions, we have modified the word:”ascetic” to “ascitic”.

11. Discussion, 4th paragraph, last sentence:
“[…] it is not recommended to use ascitic PCT testing as a stand-alone test […].”
Response: Thanks for your valuable suggestions, we have modified the word:”stand alone” to “stand-alone”.

Response: Thanks for your valuable suggestions, we have deleted the word:”ascitic PMN”

13. Discussion, 6th paragraph, last sentence: “homogeneous”.
Response: Thanks for your valuable suggestions, we have modified the word:”homogenous” to “homogeneous”.

14. Discussion, 7th paragraph, line 2: “First, in our meta-analysis […]”.
Response: Thanks for your valuable suggestions, we have modified the word:”Firstly” to “First”

15. Discussion, 7th paragraph, line 2: “First, in our meta-analysis […]”.
Response: Thanks for your valuable suggestions, we have modified the word:”Firstly” to “First”

16. Discussion, 7th paragraph, line 5: “[…] cut-off value”.
Response: Thanks for your valuable suggestions, we have modified the word:”cutoff” to “cut-off”

17. Discussion, 7th paragraph, line 7: “Second, most studies […]”.
Response: Thanks for your valuable suggestions, we have modified the word:”secondly” to “second”

18. Discussion, 7th paragraph, line 10: “Third, as mentioned […]”.
Response: Thanks for your valuable suggestions, we have modified the word:”Thirdly” to “Third”

19. Discussion, 7th paragraph, line 12: “Fourth, despite the extensive electronic search performed […]”.
Response: Thanks for your valuable suggestions, we have modified the word:”Fourthly” to “Fourth”

20. Conclusion, first sentence: “our meta-analysis […]”.
Response: Thanks for your valuable suggestions, we have modified the words:”meta analysis” to “meta-analysis”

21. Conclusion, line 3: “cut-off value”.
Response: Thanks for your valuable suggestions, we have modified the words: “cut off” to “cut-off”

Typographical errors
Comments
1. Missing space before brackets, units, numbers, or after a comma:
   Abstract: 2 occurrences.
   Introduction, first paragraph: 2 occurrences.
   Introduction, second paragraph: 6 occurrences.
   Materials and methods, data sources and search strategy: 3 occurrences.
   Materials and methods, study selection: 1 occurrence.
   Materials and methods, data extraction and quality assessment: 3 occurrences.
   Materials and methods, data synthesis and statistical analysis: 4 occurrences.
   Results, identification of studies: 1 occurrence.
   Results, study characteristics: 10 occurrences.
   Results, quality assessment: 6 occurrences.
   Results, data extraction and calculation: 3 occurrences.
   Results, diagnostic accuracy indices: 12 occurrences.
   Results, subgroup analysis: 12 occurrences.
   Results, PCT and long-term adverse outcomes of peritonitis: 3 occurrences.
   Discussion: 37 occurrences.
   Figure legends: 2 occurrences.
   Figure 1: 7 occurrences, and delete one space after “CBM”.
   Table 1: 57 occurrences, and delete one space between PCT (or CRP) and the cut-off value: 10 occurrences.
   Table 2: 56 occurrences.
Response: Thanks for your valuable suggestions, we have modified relevant contents.

2. Comma after “95% CI” or “DOR”:
   Results, diagnostic accuracy indices: 12 occurrences.
   Results, subgroup analysis: 4 occurrences.
   Response: Thanks for your valuable suggestions, we have modified these comma to colon.

3. Running title: meta-analysis
   Response: Thanks for your valuable suggestions, the running title has been modified to: “Procalcitonin in bacterial peritonitis”.
4. Abstract, results: “Fourteen studies were included in the present meta-analysis.”: add a dot at the end of the sentence.

Response: Thanks for your valuable suggestions, we have added a dot at the end of this sentence.

5. Introduction, first paragraph: “[...] micro-organisms such as Escherichia coli. The mortality of peritonitis [...] was close to 90%. With the introduction [...]”: add 2 points.

Response: Thanks for your valuable suggestions, we have added 2 points.

6. Introduction, first paragraph, line 4 to 11: the size of characters should be checked.

Response: Thanks for your valuable suggestions, the size of these characters has been unified.

7. Introduction, second paragraph, line 5 to 6: the size of characters should be checked.

Response: Thanks for your valuable suggestions, the size of these characters has been unified.

8. Introduction, second paragraph: “[...] extrathyroidal cells (e.g. monocytes)”: delete space after first bracket.

Response: Thanks for your valuable suggestions, we have deleted the space after first bracket.

9. Materials and methods, data sources and search strategy, line 2: “[...] reporting guidelines [8]. We performed a literature search [...]”: add a space after end of first sentence.

Response: Thanks for your valuable suggestions, we have added a space after end of first sentence.

10. Materials and methods, data sources and search strategy, line 8: “[...] search method used in the meta-analysis”.

Response: Thanks for your valuable suggestions, we have modified the words: “meta analysis” to “meta-analysis”


Response: Thanks for your valuable suggestions, we have deleted the space before comma, add point after last letters.

12. Materials and methods, study selection, last sentence: “[...] assessed the full-text articles independently. We presented [...]”: add a point before last
sentence.
Response: Thanks for your valuable suggestions, we have added a point before last sentence.

13. Materials and methods, data extraction and quality assessment, line 5: “[...] meta-analysis”.
Response: Thanks for your valuable suggestions, we have modified the words:” meta analysis” to “meta-analysis”

Response: Thanks for your valuable suggestions, we have added a point after last sentence.

15. Results: subtitle: “Identification of studies”.
Response: Thanks for your valuable suggestions, we have modified the words:” Identification of Studies” to “Identification of studies”

16. Results, identification of studies, line 3: “Having reviewed the full text of the remaining 139 articles, we then excluded [...]”: add a comma after “articles”.
Response: Thanks for your valuable suggestions, we have added a comma after “articles”.

17. Results: subtitle: “Study characteristics”.
Response: Thanks for your valuable suggestions, we have modified the words:” Study Characteristics” to “Study characteristics”.

18. Results: subtitle: “Quality assessment”.
Response: Thanks for your valuable suggestions, we have modified the words:” Quality Assessment” to “Quality assessment”.

19. Results: subtitle: “Data extraction and calculation”.
Response: Thanks for your valuable suggestions, we have modified the words:” Data Extraction and Calculation” to “Data extraction and calculation”.

20. Results, diagnostic accuracy indices, line 1-2: “A total of 13 studies [...]”.
Response: Thanks for your valuable suggestions, we have modified the words:”a” to:”A”.

21. Results, diagnostic accuracy indices, second paragraph, line 2: “[...] value of serum CRP levels [...]”. The pooled sensitivity for CRP [...]”: add a point at the end of the sentence.
Response: Thanks for your valuable suggestions, we have added a point at the end of the sentence.
22. Results, diagnostic accuracy indices, 4th paragraph, line 2: “[...] across all settings. We found that the diagnostic OR was [...]”: add a point at the end of the sentence.
Response: Thanks for your valuable suggestions, we have added a point at the end of the sentence.

23. Results, diagnostic accuracy indices, 4th paragraph, line 5: “[...] respectively. The pooled positive likelihood ratio [...]”: add a point at the end of the sentence.
Response: Thanks for your valuable suggestions, we have added a point at the end of the sentence.

24. Results, subgroup analysis, 2nd paragraph, line 6: “[...] PCT in cirrhotic patients. The pooled sensitivity [...]”: add a point at the end of the sentence.
Response: Thanks for your valuable suggestions, we have added a point at the end of the sentence.

25. Results: subtitle: “PCT and long-term adverse outcomes of peritonitis”.
Response: Thanks for your valuable suggestions, we have modified the words:”Peritonitis” to “peritonitis”.

26. Results, PCT and long-term adverse outcomes of peritonitis, first sentence: “Only two studies”.
Response: Thanks for your valuable suggestions, we have modified the words:”Two” to “two”.

27. Results, PCT and long-term adverse outcomes of peritonitis, line 4: “However, Connert et al. [...]”.
Response: Thanks for your valuable suggestions, we have modified the words:”et,al.” to “et al.”.

28. Discussion, 1st paragraph, line 2-3: “[...] long half-life of 25-30 h [3]. It was first identified [...] hypocalcaemia associated with [...]”: add a point at the end of the sentence, and correction.
Response: Thanks for your valuable suggestions, we have modified the words:”associate” to “associated” and added a point at the end of the sentence.

29. Discussion, 1st paragraph, line 5-6: “[...] patients with bacterial infection. It is most commonly produced from neuroendocrine cells in non-thyroidal tissues such as lung [...]”: add a point at the end of the sentence, and correction.
Response: Thanks for your valuable suggestions, we have modified the words:”tissue” to “tissues” and added a point at the end of the sentence.

30. Discussion, 1st paragraph, line 8: “[...] or sterile inflammation. In the serum
31. Discussion, 2nd paragraph, line 13: “[…] by Opatrna et al. […]”.
Response: Thanks for your valuable suggestions, we have modified the words: “et, al” to “et al.”

32. Discussion, 7th paragraph, line 5: “[…] cut-off value effect. Despite the adjustment […]”: delete a space after the point.
Response: Thanks for your valuable suggestions, we have deleted a space after the point.

33. References:
The space between issue number and the double point should be deleted in the following references: [10], [11], [15], [16], [25], [26], [27], [28], [29], [33], [34], [38],[40], [41], [42].
Response: Thanks for your valuable suggestions, the format of the references was rectified in order to conform to the BMC Infectious Diseases style.

34. References:
[24]: “TNFa and IL-6”: add a space.
[26]: “TNFa and LPS”: add a space.
Response: Thanks for your valuable suggestions, the format of the references was rectified in order to conform to the BMC Infectious Diseases style.

35. Table 1: “Cut-off”.
Response: Thanks for your valuable suggestions, we have modified the words:” Cutoff” to “Cut-off.”

37. Table 2, footnote a: “High cut-off value”.
Response: Thanks for your valuable suggestions, we have modified the words:” Cutoff” to “Cut-off.”

Grammatical errors
Comments
1. Introduction, first paragraph: “It frequently occurs in […] patients receiving continuous ambulatory peritoneal dialysis therapy”.
Response: Thanks for your valuable suggestions, we have modified the words:” receive” to “receiving.”
2. Introduction, second paragraph: “[…] their ability to diagnose bacterial infections, […]”.
Response: Thanks for your valuable suggestions, we have modified the words: “infection” to “infections.”

3. Introduction, second paragraph: “[…] produced by extrathyroidal cells (e.g. monocytes)”
Response: Thanks for your valuable suggestions, we have modified the words: “extrathyroide” to “extrathyroidal.”

4. Introduction, second paragraph, last sentence: “[…] we calculated the summary receiver operating characteristic (ROC) curve […]”.
Response: Thanks for your valuable suggestions, we have modified the words: “calculate” to “calculated.”

5. Materials and methods, data synthesis and statistical analysis, line 9-10: “[…] area under the receiver operating characteristic curves (AUROC), irrespective of the different cut-off points used”.
Response: Thanks for your valuable suggestions, we have modified the words: “Cutoff” to “Cut-off.”

6. Results, identification of studies, line 4-8: “[…] among them, 46 were review articles; 22 were case reports; 8 were animal studies; 5 did not investigate the diagnostic value of serum PCT level; and 34 were not in English or Chinese in the text; 4 were retrospective studies, and 6 studies were unable to reconstruct 2×2 tables. Finally, 14 eligibility studies were included in the analysis”.
Response: Thanks for your valuable suggestions, We have added four new trials after researched from multiple databases, and some words has been modified in the chapter of Identification of studies, please check it.

7. Results, quality assessment, line 9-10: “[…] lead to potential spectrum bias existed. […] or uninterpretable results. Seven studies did not state whether the PCT results were interpreted without knowledge of outcome assessment […]. It was poorly reported […].”
Response: Thanks for your valuable suggestions, we have modified the words: “know” to “knowledge.”

8. Results, diagnostic accuracy indices, 4th paragraph, line 2: “[…] We found that the diagnostic OR was […]”.
Response: Thanks for your valuable suggestions, we have modified the words: “of” to “was.”
9. Results, subgroup analysis, 1st paragraph, line 2: “Four studies […] reported test results […]”.
Response: Thanks for your valuable suggestions, we have modified the words:”reporting” to “reported.”

10. Results, subgroup analysis, 1st paragraph, last sentence: “[…] showed slightly decreased sensitivity, but increased specificity […]”.
Response: Thanks for your valuable suggestions, we have deleted the word:”in”

11. Discussion, 2nd paragraph, line 10: “[…] new reliable diagnostic markers such as PCT […]”.
Response: Thanks for your valuable suggestions, we have modified the words:”marker” to “markers.”

12. Discussion, 4th paragraph, line 8: “[…] and PCT was not synthesized by leucocytes […]”.
Response: Thanks for your valuable suggestions, we have modified the words:”is” to “was

13. Figure legends: Figure 5: “[…] diamond shape, and the respective […]”: add a comma.
Response: Thanks for your valuable suggestions, we have added a comma.

Stylistic suggestions
Comments
1. Key words: “[…]; and meta-analysis”: the “and” should be deleted.
Response: Thanks for your valuable suggestions, we have deleted the words:”and”.

2. Abstract, background: “Many studies have highlighted the potential usefulness of procalcitonin”.
Response: Thanks for your valuable suggestions, we have modified the words:”illuminated the” to “highlighted the potential”

3. Abstract, methods: “We performed a systematic review in multiple databases to identify studies that evaluated […]”.
Response: Thanks for your valuable suggestions, the sentence has been modified to:” We performed a systematic searched from MEDLINE, EMBASE, SCOPUS, China Biology Medicine Database(CBM), and China National Knowledge Infrastructure Database(CNKI) and Cochrane databases…”

4. Abstract, results: “Fourteen studies were included in the present meta-analysis.”
Response: Thanks for your valuable suggestions, the sentence has been modified to:” Eighteen studies involving 1827 patients were included in the present meta-analysis…”

5. Abstract, results: “The pooled sensitivity and specificity of serum PCT for the diagnosis of peritonitis […].”
Response: Thanks for your valuable suggestions, we have modified the words:” diagnosing” to “the diagnosis”.

6. Abstract, results: Use of higher PCT cut-off values could improve […].
Response: Thanks for your valuable comments on our paper, we have added four new trials after researching relevant trials, the subgroup analysis result showed that the diagnostic value using common PCT cut-offs (0.5ng/ml) was higher compared with that using of higher PCT cut-off values (Table 2). So the words:”high” has been replaced with:”common”.

7. Abstract, conclusions: “However, with regard to methodological limitations and significant heterogeneity between studies, […]”.
Response: Thanks for your valuable suggestions, we have modified the words:”as” to “with regard to”.

8. Introduction, first paragraph: “However, it is still a common illness that adversely affects the prognosis, […].”
Response: Thanks for your valuable suggestions, the sentence has been modified to:” it is still a common illness that adversely affects the prognosis…”

9. Introduction, first paragraph: “It frequently occurs in children and adults, and can endanger life, particularly in patients with decompensated cirrhosis or in patients receiving continuous ambulatory peritoneal dialysis therapy”. 
Response: Thanks for your valuable suggestions, we have modified the words:” receive” to “receiving”.

10. Introduction, first paragraph: “Consequently, diagnosis of bacterial peritonitis continues to be a major clinical challenge, and an accurate biomarker for the early identification of peritonitis would be of great diagnostic value.
Response: Thanks for your valuable suggestions, the sentence has been modified to:” Consequently, diagnosis of bacterial peritonitis continues to be a major clinical challenge, and an accurate biomarker for the early identification of peritonitis would be of great diagnostic value.”

11. Introduction, second paragraph, line 5: “There is some evidence indicating a good diagnostic accuracy of the PCT test […].”
Response: Thanks for your valuable suggestions, we have modified the words:” indicates” to “indicating a”. 
12. Introduction, second paragraph, line 11: “Additionally, several new studies of procalcitonin [...]”.
Response: Thanks for your valuable suggestions, we have modified the words: “a lot of” to “several”.

13. Introduction, second paragraph, line 12-14: “Therefore, we undertook the present systematic review and meta-analysis mainly to quantitatively summarize the current evidence about PCT as a marker [...]”.
Response: Thanks for your valuable suggestions, the sentence has been modified to: “Therefore, we undertook the present systematic review and meta-analysis mainly to…”

14. Introduction, second paragraph, last sentence: “Because there is no consensus […], and as different PCT thresholds have been used between studies, we calculated summary receiver operating characteristic (ROC) curves approach to perform […].
Response: Thanks for your valuable suggestions, the sentence has been modified to: “and as different PCT thresholds have been used between studies, we calculated summary receiver operating characteristic (ROC) curves approach to perform…”

15. Materials and methods, data sources and search strategy, line 2-5: “We performed a literature search in MEDLINE, […], Cochrane databases, China Biology Medicine database (CBM), and China National Knowledge Infrastructure (CNKI) databases […].
Response: Thanks for your valuable suggestions, the sentence has been modified to: “We performed a literature search in MEDLINE…”

16. Materials and methods, data sources and search strategy, line 9: “[…] and unpublished studies were sought initially without language restrictions”.
Response: Thanks for your valuable suggestions, the sentence has been modified to: “and unpublished studies were sought initially without language restrictions”.

17. Materials and methods, data sources and search strategy, last sentence: “[…] in order to identify other potentially relevant trials”.
Response: Thanks for your valuable suggestions, the sentence has been modified to: “in order to identify other potentially relevant trials”.

18. Materials and methods, study selection, first sentence: “Only studies that investigated the diagnostic accuracy […].
Response: Thanks for your valuable suggestions, the sentence has been modified to: “Only studies that investigated the diagnostic accuracy […].
19. Materials and methods, study selection, line 4-5: “[…], we only included articles published in English and Chinese although there was no language restrictions”.
Response: Thanks for your valuable suggestions, the sentence has been modified to: “we only included articles published in English and Chinese although there was no language restrictions”.

20. Materials and methods, data synthesis and statistical analysis, line 3-4: “[…] diagnostic odds ratio (DOR) and the likelihood ratio et al. based on the bivariate random effect […]”.
Response: Thanks for your valuable suggestions, we have been modified the words: “effects” to “effect”.

21. Materials and methods, data synthesis and statistical analysis, line 9-10: “[…] area under the receiver operating characteristic curves (AUROC), irrespective of the different cut-off points used”.
Response: Thanks for your valuable suggestions, the sentence has been modified to: ”area under the receiver operating characteristic curves (AUROC), irrespective of the different cut-off points used”.

22. Results, study characteristics, line 4-7: “All studies were conducted in adult patients: 4 of them referred to peritoneal dialysis patients […]; 9 studies reported spontaneous bacterial peritonitis in cirrhotic patients […] and 1 study in chronic severe hepatitis patients [...]”.
Response: Thanks for your valuable suggestions, the sentence has been modified to: ”4 of them referred to peritonitis in peritoneal dialysis patients…”

23. Results, study characteristics, line 10-12: “Common bacteria isolated were Escherichia coli, and Streptococcus species. PCT levels were measured in serum samples in 13 studies […], and in ascitis fluid samples in 4 studies […].”
Response: Thanks for your valuable suggestions, the sentence has been modified to: ”Common bacteria isolated were Escherichia coli, and Streptococcus species…”

24. Results, data extraction and calculation, line 3-6: “PCT measurement was performed at the beginning of the trial in most of the included studies. We reported the PCT and CRP cut-off values in Table 1. Cut-off values for serum or ascitic PCT varied between studies, ranging from 0.38-13.7 ng/ml, or 0.3-10 ng/ml, respectively”.
Response: Thanks for your valuable suggestions, the sentence has been
modified to:” PCT measurement was performed at the beginning of the trial in most of the included studies. We reported the PCT and CRP cut-off values in Table 1. Cut-off values for serum or ascitic PCT varied between studies, ranging from 0.42-13.7 ng/ml, or 0.3-10 ng/ml, respectively”

25. Results, diagnostic accuracy indices, line 1-3: a shorter sentence is better:
“A total of 13 studies […] have investigated the diagnostic value of PCT in serum. Our analysis indicated that serum PCT has a high degree of accuracy for the diagnosis of peritonitis”.
Response: Thanks for your valuable suggestions, the sentence has been modified to:” A total of 17 studies […] have investigated the diagnostic value of PCT in serum. Our analysis indicated that serum PCT has a high degree of accuracy for the diagnosis of peritonitis”

26. Results, subgroup analysis, 2nd paragraph, last sentence: “[…] AUROC was 0.87 […], indicating that serum PCT […]”.
Response: Thanks for your valuable suggestions, the words:"it indicated" has been modified to :"indicating".

27. Results, PCT and long-term adverse outcomes of peritonitis, line 5: “[…] cirrhotic patients with PCT levels above […].”
Response: Thanks for your valuable suggestions, the words:" the level of PCT" has been modified to :" PCT levels”.

28. Discussion, 2nd paragraph, line 1-4: “There are many types of bacterial peritonitis. In clinical practice, they are most commonly found in patients with peritoneal dialysis (PD), and in cirrhotic patients. PD represents an important treatment option for […]”.
Response: Thanks for your valuable suggestions, the words:" among them" has been modified to :" In clinical practice”.

29. Discussion, 2nd paragraph, line 7-9: “Microbiological culture system in PD effluent is the gold standard for diagnosis of PD-associated peritonitis, but suffers from […]”.
Response: Thanks for your valuable suggestions, the words:" suffer” has been modified to :” suffers”.

30. Discussion, 2nd paragraph, line 12-13: “[…] is the major pathway for clearance of PCT [36]”
Response: Thanks for your valuable suggestions, the words:" elimination” has been modified to :” clearance”.

31. Discussion, 2nd paragraph, line 16-19: “[…] PCT correlated weakly with
renal function dysfunction, and […] based on PCT [36,38]. Our meta-analysis also confirmed a quite favorable diagnostic accuracy of high PCT values in PD patients […]”.

Response: Thanks for your valuable suggestions, the sentence has been modified to:” Our meta-analysis also confirmed an acceptable diagnostic accuracy for PCT testing in PD patients”.

32. Discussion, 3rd paragraph, line 5-6: “There is considerable evidence indicating that high PCT levels may be related to infections in cirrhosis [23]. Although the liver is considered as the main source […]”.

Response: Thanks for your valuable suggestions, the sentence has been modified to:” There is considerable evidence indicating that high PCT levels may be related to infections in cirrhosis…”

33. Discussion, 3rd paragraph, last sentence: “[…] PCT testing has a good accuracy for the diagnosis of bacterial peritonitis in cirrhotic patients […]”.

Response: Thanks for your valuable suggestions, the sentence has been modified to:” PCT testing has a good accuracy for the diagnosis of bacterial peritonitis in cirrhotic patients”.

34. Discussion, 4th paragraph, first sentence: “Some authors postulated that ascitic PCT might be more sensitive than serum PCT […], because bacterial infection could trigger peritoneal inflammatory cells […]”.

Response: Thanks for your valuable suggestions, the sentence has been modified to:” Some authors postulated that ascitic PCT might be more sensitive than serum PCT […], because bacterial infection could trigger peritoneal inflammatory cells […]”.

35. Discussion, 4th paragraph, line 4-5: “In the present study, the pooled analysis of 4 studies […] suggested that ascitic PCT […] could be a more accurate test […]”.

Response: Thanks for your valuable suggestions, the sentence has been modified to:” In the present study, the pooled analysis of 5 studies[21, 22, 27, 28, 33] suggested that ascitic PCT…”

36. Discussion, 4th paragraph, last sentence: “[…] it is not recommended to use ascitic PCT testing as a stand-alone test, and […] to fully elucidate the potential diagnostic value of ascitic PCT”.

Response: Thanks for your valuable suggestions, the sentence has been modified to:” it is not recommended to use ascitic PCT testing as a stand-alone test…”

37. Discussion, 5th paragraph, line 2-4: “In a virtual population with a 20%
prevalence of peritonitis (the actual prevalence [...] ), use of a serum PCT test [...] ".
Response: Thanks for your valuable suggestions, the sentence has been modified to: "In a virtual population with a 20% prevalence of peritonitis".

38. Discussion, 5th paragraph, line 10: "Using data from the subgroup with a higher PCT [...] ".
Response: Thanks for your valuable suggestions, the sentence has been modified to: "Using data from the subgroup with a higher PCT".

39. Discussion, 5th paragraph, last sentence: "[...] a negative post-test probability or 7%. Therefore, higher PCT cut-off values may be a more useful [...] ".
Response: Thanks for your valuable suggestions, the sentence has been modified to: "Therefore, higher PCT cut-off values may be a more useful".

40. Discussion, 6th paragraph, first and 2nd sentences: "[...] for the overall results between the fourteen included studies. Potential source of heterogeneity included the different characteristics of the studies, such as methodological quality, prevalence of case patients (range from 0.1 to 0.74), size of the study populations, different reference standards in PD [...] ".
Response: Thanks for your valuable suggestions, the sentence has been modified to: "Here was substantial heterogeneity detected for the overall results between the eighteen included studies...".

41. Discussion, 6th paragraph, line 8-11: "Other unrecorded differences among these studies may also contribute to the heterogeneity. Evaluation of individual patient data or meta-regression would help in this analysis of the sources of heterogeneity".
Response: Thanks for your valuable suggestions, the sentence has been modified to: "Other unrecorded differences among these studies may also contribute to the heterogeneity. Evaluation with individual patient data or meta-regression would help in this analysis of the sources of heterogeneity".

42. Discussion, 6th paragraph, line 13: "[...] it limits our ability to further evaluate heterogeneity".
Response: Thanks for your valuable suggestions, the sentence has been modified to: "It limits our ability to further evaluate heterogeneity".

43. Discussion, 6th paragraph, last sentence: "On the other hand, using more homogeneous trials could solve this difficulty, but could induce selections bias".
Response: Thanks for your valuable suggestions, the sentence has been
modified to:” On the other hand, using more homogeneous trials could solve this difficulty, but could induce selections bias

44. Discussion, 7th paragraph, line 3-4: “[…] specificities varied between studies. We constructed the ROC curve […].”
Response: Thanks for your valuable suggestions, the words:”among” has been modified to:”between”.

45. Discussion, 7th paragraph, line 7-9: “[…] most studies have a case-control design. It has been demonstrated that case-control studies could over-estimate the accuracy of a diagnostic test [42], therefore more larger prospective trials should be performed to elucidate […].”
Response: Thanks for your valuable suggestions, the sentence has been modified to:” most of the studies have a case-control design, it has been demonstrated that the case-control design could over-estimate the accuracy of a diagnostic test[50], therefore more larger prospective trials should be performed“.

46. Discussion, 7th paragraph, line 10-12: “[…] our study suffered from moderate heterogeneity, mainly owing to different patients characteristics, and different definitions of peritonitis.
Response: Thanks for your valuable suggestions, the sentence has been modified to:” our study suffered from moderate heterogeneity, mainly owing to different patients characteristics, and different definitions of peritonitis.

47. Discussion, 7th paragraph, last sentence: “[…] especially because positive studies are more easily reported“. 
Response: Thanks for your valuable suggestions, the sentence has been modified to:” especially because positive studies are more easily reported“

48. Conclusion, line 1-3: “Our meta-analysis showed that PCT is a helpful marker in identifying bacterial peritonitis. Although PCT performs as well in PD patients as in cirrhotic or severe hepatitis patients, use of a higher cut-off value […]”. 
Response: Thanks for your valuable suggestions, the sentence has been modified to:” our meta-analysis shows that PCT is a helpful marker in identifying bacterial peritonitis, Although PCT performs as well in PD patients as in cirrhotic or severe hepatitis patients, use of a common cut-off value may further enhance accuracy.”

49. Conclusion, line 5-7: “However, it is important to note that PCT cannot be recommended as a “gold standard” test for peritonitis up to now, and should be interpreted in combination with other clinical, analytical, and/or microbiological data. Given the limits of PCT as a single marker, additional large prospective
studies should determine its diagnostic value in bacterial peritonitis, when interpreted in association with other biomarkers”.

Response: Thanks for your valuable suggestions, the sentence has been modified to: “However, it is important to note that PCT cannot be recommended as a “gold standard” test for peritonitis up to now, and should be interpreted in combination with other clinical, analytical, and/or microbiological data. Given the limits of PCT as a single marker, additional large prospective studies should determine its diagnostic value in bacterial peritonitis, when interpreted in association with other biomarkers.”.

We thank the reviewers and the editors very much for the comments which make us think and learn a lot, and believe that the amendments will make this manuscript more valuable. We hope the reviewers and the editors will be satisfied with the revisions for the original manuscript.

If you have any question about this paper, please don’t hesitate to let us know.

Thanks and best regards!

Yours sincerely,

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