

We would like to express our sincere thanks to the reviewers for the constructive and positive comments.

Replies to Reviewer 1

1. In designing this prospective study, how did the authors calculate sample size ?

Answer: According to previous research sample size of others, we choose case income sample size 1 year.

2. Please provide the references for diagnostic criteria of ITB.

Answer: 1. identification of mycobacterium tuberculosis (MTB) by acid-fast staining or culture in biopsied specimens; 2. presence of caseating granulomas in histological examination; 3. improvement of clinical and endoscopic disease activity after at least 3 months of anti-TB therapy. (page 5, paragraph 2, line 4)

3. Please present the detailed method and positive criteria for PPD test.

Answer: The detailed method: Select tuberculin purified protein derivative 1 and physiological saline solution 1, with 1 ml syringe take concentrate 0.1 ml diluted saline to 0.25 ml, patients around the forearm medial intradermal injection of 0.1 ml. Positive criteria: Scleroma average

diameter, such as negative for less than 5 mm, greater than or equal to 5 mm less than 20 mm for positive reaction, more than 20 mm (+ + +) or local have blisters, necrosis, lymphangitis are strong positive. (page 2, paragraph2, line4)

4. The endoscopic, pathologic, and radiologic evaluation (CTE) could be subjective. How were they performed ? Were they performed by more than two independent blinded researchers ? Please describe the detailed methods.

Answer: We chose a deputy chief physician specializes in research, respectively in endoscopy, pathological and imaging, all the results will be determined after two chief physician for review. The endoscopic evaluation is performed by Zhu X and Liao WD, the pathologic evaluation is performed by Tu Y and Tao XQ, the radiologic evaluation is performed by Yu C and Gong HH.

5. What is the "intestinal diseases" in CTE? Did this mean small bowel involvement ?

Answer: Yes, it means that the small bowel involvement

6. The authors did not present and compare the results of chest X-ray. Active or past TB lesions in chest X-ray could be very helpful in

differential diagnosis between CD and ITB. It is also very simple and cheap to perform.

Answer: Thank you for your reminder , we have compared the results of chest X-ray. They are not statistically significant, so we put it out.

7. Did the authors perform ASCA test in this study ? It also could be helpful in differential diagnosis between two diseases.

Answer: Thank you for your advice , our hospital can't perform ASCA test, so we don't choose it.

8. How did the authors select 12 variables to make a scoring system among 16 variables in table 2?

Answer: The 12 variables have high specificity, more than eighty-five percent, their P value is less than 0.05, with statistical significance.

9. The results from 65 patients should be validated in the independently enrolled validation set. However, it was not presented.

Answer: This was the first time we did prospective experiment, We didn't validate in the independently enrolled validation set due to lack of experience. Next time we must be validated in the independently enrolled validation set before the experiment. The study is a public welfare fund

projects of the ministry of health by the affiliated hospital of Sun Yat-Sen University.

10. In discussion section, the proposed relationship between diseases and job does not seem to be so persuasive. More evidence or references should be added.

Answer: The proposed relationship between diseases and job does not seem to be so persuasive, lack of samples might be the reason, increasing the sample might be able to solve this problem. In China, the living condition of farmers are poor, they are more likely to suffer from intestinal tuberculosis, it could also be a reason

Replies to Reviewer 2

1. The test T spot TB is mentioned without any explanation.

Answer: T-SPOT.TB is an interferon-gamma release assay to detect T-cell response to early secreting antigen target 6 and culture filtrate protein 10 peptides by enzyme-linked immunospot assay for tuberculosis diagnosis. It is highly sensitive and specific, and will not be affected by the subject's immune status and Bacillus Calmette-Guerin vaccination. (page 2, paragraph 2, line 12)

2. In patients and methods the following sentence is not clear “Of the 80 patients, 12 patients were lost to follow-up before the diagnosis was confirmed, 0 patient were diagnosed both CD and ITB and 3 patients were diagnosed neither CD nor ITB”.

Answer: In the 80 patients into the group, 12 of the 80 patients lost to follow-up at last, 3 of the 80 patients were diagnosed neither CD nor ITB, So accurate diagnosis of the patients are 65 at last.

3. The authors have selected cases in which the differentiation was not possible and trial of anti TB treatment was given. However, in drug resistant TB there may not be response in 2 to 3 month. Authors should mentioned in how many patients with ITB.

Answer: Thank you very much for your advice, in our study, some patients with intestinal tuberculosis anti-tuberculosis treatment was invalid after 3 months, but they were better after hormone treatment. It is proved that they should be crohn disease, rather than resistance of intestinal tuberculosis.

4. How was the weightage for each variable decided? It is not possible that each variable has same weightage.

Answer: We really aware of the problem, because our sample size is too

little, the statistics teacher considered that we can not use for statistical regression analysis, So we referred to the study of Lee *et al.*

Replies to Reviewer 3

1. Please describe the details of study design. Authors said that this study was prospective. However, detailed protocols including inclusion and exclusion criteria were not commented. Also, the details of laboratory and radiologic exams such as TSPOT, PPD, Labs and CTE should be described in Methods.

Answer: T-SPOT.TB is an interferon-gamma release assay to detect T-cell response to early secreting antigen target 6 and culture filtrate protein 10 peptides by enzyme-linked immunospot assay for tuberculosis diagnosis. It is highly sensitive and specific, and will not be affected by the subject's immune status and Bacillus Calmette-Guerin vaccination. (page 2, paragraph 2, line 12) ;

PPD test: Select tuberculin purified protein derivative 1 and physiological saline solution 1, with 1 ml syringe take concentrate 0.1 ml diluted saline to 0.25 ml, patients around the forearm medial intradermal injection of 0.1 ml. Positive criteria: Scleroma average diameter, such as negative for less than 5 mm, greater than or equal to 5 mm less than 20 mm for

positive reaction, more than 20 mm (+++) or local have blisters, necrosis, lymphangitis are strong positive. (page 2, paragraph2, line4) ;

CTE: The patient is asked to arrive one hour prior to the exam. Three bottles (1350 mL) of negative oral contrast (VoLumen) will be given to the patient to drink 45 minutes, 30 minutes and 15 minutes prior to the exam. The patient will lie fully clothed on the exam table. The scan time is approximately 5 minutes, during which time the patient is given an IV injection of non-ionic contrast.

2. Authors said that CD patients who had not received infliximab & AZA/6-MP/MTX were included. However, I think that study patients also should not be received steroids to be included in this study because steroids may affect the results of AFB culture (An important inclusion criteria of this study).

Answer: This is a very good advice, in our study, we found that CD patients who had not received AZA/6-MP/MTX were not received steroids at the same time. So there is no affect the results.

3. Diagnostic criteria for ITB included improvement of clinical and endoscopic disease activity after at least 3 months of anti-TB therapy. However, the very next sentence said 'anti-tuberculous therapy was tried for 2-3 months'. Which one was correct? 3 months or 2-3 months? Please

clarify this.

Answer: This is our writing mistake, it is 3 months, we have modified.

4. In this study, clinical response to anti-TB medication was defined as loss of subjective symptoms. However, I think this definition was too vague to use in this prospective design.

Answer: Clinical response is subjective, but in addition to the clinical response, we also would see other indicators, especially the performance of endoscopic.

5. In the results of CTE section, what do you mean by 'intestinal disease'? It is too vague.

Answer: It means that the small bowel involvement .

6. In results section, please add the flowchart of patients' inclusion & exclusion.

Answer: Ok, we have add the flowchart of patients' inclusion & exclusion. (Table 4 Part1)

7. Finally authors developed scoring system of CD and ITB. I think it is better if authors show the scoring system as a diagram.

Answer: Ok, we have add the diagram of the scoring system. ((Table 4

Part2)

8. In discussion, authors cited study from Lee YJ et al. However, their scoring system did not use 'endoscopic ultrasonography'. Please double-check this.

Answer: Yes, this is our mistake, we have modified.

9. The English in this paper should be revised by a native speaker.

Answer: I know my English is not good, I hope the WJG can help me to modify the English, I'll be responsible for the cost, thanks!

We would like to express our sincere thanks to the Journal Editor Chief for the constructive and positive comments.

Replies to Journal Editor Chief

1、 How the CTE evaluation was performed?

Answer: The CTE could be subjective, so two independent blinded researchers were chosen for review in each CTE. They will analyze the positive results, and will discuss with chief physician if an agreement cannot be reached. CTE check showed the patients with CD or ITB had thickening bowel walls, so the evaluation of its was performed by intestinal fistula, target sign, comb sign, lymph node strengthening. The patients with intestinal diseases, intestinal fistula, target sign (Figure 4) or comb sign (Figure 3) were more commonly seen in CD patients, they were 19 cases (76%) , 9 cases (36%) , 13 cases (52%) and 12 cases (48%) . They had significantly difference ($P < 0.05$). The 8 cases patients with lymph node strengthening had ITB, they were not statistically significant ($P > 0.05$). (page 9, paragraph4)

2、 why chest X-ray results were not included in the scoring system?

Answer: Active or past TB lesions in chest X-ray and PPD could be very helpful in differential diagnosis between CD and ITB. In our study, all patients have made chest X-ray and PPD, but only three positive patients in chest X-ray, they are not statistically significant ($P > 0.05$), so we put it out and don't selecte it to establish our scoring system. There are forty-one positive patients in PPD, they are statistically significant ($P < 0.05$), so we select it. (page 6, paragraph5)

3、 The details of the PPD test.

Answer: The detailed method for PPD test: Select tuberculin purified protein derivative 1 ml and physiological saline solution 1 ml, with 1 ml syringe take concentrate 0.1 ml diluted saline to 0.25 ml, patients around the forearm medial intradermal injection of 0.1 ml. Positive criteria: It is positive + if

scleroma diameter is more than 5mm but less than or equal to 10mm; it is positive ++ if scleroma diameter is more than 10mm but less than or equal to 20mm; it is positive +++ (strong positive) if scleroma diameter is more than 20mm or local have blisters, necrosis or lymphangitis; It is negative if scleroma diameter is less than 5mm. (page 6, paragraph6)

4、 The grammar is technically correct, but the sentence structure is convoluted and difficult to read.

Answer: We know English is not our native language. The AJE would help us to revise the English again.