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OPEN PEER REVIEW

Correlation Between CD4 Cell Count, HIV Viral Load, and Chest CT Findings of AIDS-associated Pulmonary Cryptococcosis

Zixin Zhang, Chunshuang Guan, Budong Chen, Ruming Xie

SUBMITTED	REVISED	ACCEPTED	DOI
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About this report

This open peer review (OPR) report shows the public comments made on this article during peer review, by the reviewers, the associate editor and the editor-in-chief, for every revision round, together with the authors' replies. Comments appear only with the consent of the people who wrote them. Reviewers who chose to sign their report are named; the others are shown as "Referee". Comments are edited for language only, and confidential remarks to the editors are not included.

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1 Original submission

1 comment · 25 Apr 2022

Editor-in-Chief

MINOR REVISION 25 Apr 2022

Dear authors,
Before starting the review process for your article, it is necessary to clarify the following items:

- Please provide the ethics code and the web address. If the web address (link) for the ethics committee approval is not available, please upload the official approval document from your ethics committee.

- Please clarify the funding source and provide the web address or upload the official grant approval number.

- Regarding the importance of “conflict of interest” clarification, the corresponding author should fill out the “ICMJE form” and upload it during the submission process. (The form is available in the “conflict of interest” section of the site:
https://brief.land/iranjradiol/knowledgebase/category/tree.html#conflicts_of_interest.html).
Regards

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Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

EIC Decision:

-Please mention the ethical code with the link address. If the web address (link) of ethical committee approval is not available, please upload the official approval document of your ethics committee.

The ethical code has been mentioned in that section. Thank you so much.

- Please clarify the financial resource with the link address or upload the official approval grant number.

The official approval grant number has been mentioned in that section. Thank you so much.

-Regarding the importance of “conflict of interest” clarification, the corresponding author should fill out the “ICMJE form” form and upload in the submission process.

The ‘ICMJE form” form is as follows :

ICMJE COI FORM

Date:	5/5/2022
Your Name:	Xie Ruming
Manuscript Title:	The correlation between CD4 cell count, HIV viral load and the chest CT findings in A associated pulmonary cryptococcosis
Manuscript Number (if known):	ID 127182

In the interest of transparency, we ask you to disclose all relationships/activities/interests listed below that are related to the co of your manuscript. “Related” means any relation with for-profit or not-for-profit third parties whose interests may be affect

the content of the manuscript. Disclosure represents a commitment to transparency and does not necessarily indicate a bias. I are in doubt about whether to list a relationship/activity/interest, it is preferable that you do so.

The author's relationships/activities/interests should be defined broadly. For example, if your manuscript pertains t epidemiology of hypertension, you should declare all relationships with manufacturers of antihypertensive medication, even i medication is not mentioned in the manuscript.

In item #1 below, report all support for the work reported in this manuscript without time limit. For all other items, the time f for disclosure is the past 36 months.

		Name all entities with whom you have this relationship or indicate none (add rows as needed)	Specifications/Comments (e.g., if payments were made to you or to your institution)
Time frame: Since the initial planning of the work			
1	All support for the present manuscript (e.g., funding, provision of study materials, medical writing, article processing charges, etc.) **No time limit for this item.**	☒ **None**	
			Click the tab key to add additional rows.
Time frame: past 36 months			
2	Grants or contracts from any entity (if not indicated	☒ **None**	

		Name all entities with whom you have this relationship or indicate none (add rows as needed)	Specifications/Comments (e.g., if payments were made to you or to your institution)
	in item #1 above).		
3	Royalties or licenses	☒ **None**	
4	Consulting fees	☒ **None**	
5	Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events	☒ **None**	
6	Payment for expert testimony	☒ **None**	
7	Support	☒ **None**	

		Name all entities with whom you have this relationship or indicate none (add rows as needed)	Specifications/Comments (e.g., if payments were made to you or to your institution)
	for attending meetings and/or travel		
8	Patents planned, issued or pending	☒ **None**	
9	Participation on a Data Safety Monitoring Board or Advisory Board	☒ **None**	
10	Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid	☒ **None**	
11	Stock or stock options	☒ **None**	

		Name all entities with whom you have this relationship or indicate none (add rows as needed)	Specifications/Comments (e.g., if payments were made to you or to your institution)
12	Receipt of equipment, materials, drugs, medical writing, gifts or other services	☒ **None**	
13	Other financial or non-financial interests	☒ **None**	

Please place an "X" next to the following statement to indicate your agreement:

☒ I certify that I have answered every question and have not altered the wording of any of the questions on this form.

2 Revision 1

1 comment · 14 May 2022

Editor-in-Chief

MINOR REVISION 14 May 2022

Dear authors,
Before starting the review process for your article, it is necessary to clarify the following items:

Please mention the ethics code and provide the link. If the web address (link) for the ethics committee approval is not available, please upload the ethics committee's official approval document.

Please upload the following file (ICMJE) separately:
Given the importance of clarifying “conflict of interest,” the corresponding author should fill out the “ICMJE form” and upload it during the submission process. (The form is available in the “conflict of interest” section of the site: https://brief.land/iranjradiol/knowledgebase/category/tree.html#conflicts_of_interest.html).
Regards

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Revision 2

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

EIC Decision:

-Please mention the ethical code with the link address. If the web address (link) of ethical committee approval is not available, please upload the official approval document of your ethics committee.

The ethical code has been mentioned in that section. Thank you so much.

- Please clarify the financial resource with the link address or upload the official approval grant number.

The official approval grant number has been mentioned in that section. Thank you so much.

-Regarding the importance of “conflict of interest” clarification, the corresponding author should fill out the “ICMJE form” form and upload in the submission process.

The ‘ICMJE form” form is as follows :

3 Revision 2

2 comments · 10 Jul 2022 – 24 Jul 2022

Referee 1 Reviewer

MINOR REVISION 10 Jul 2022

The manuscript entitled " The correlation between CD4 cell count, HIV viral load and the chest CT findings in AIDS-associated pulmonary cryptococcosis " evaluated the correlation between chest CT findings of pulmonary cryptococcosis and HIV viral load in 63 patients and the association between dynamic changes in imaging and CD4 count in 40 patients.
The study is well designed and is appropriate for publication with some revision.
My comments are as follows:
1- The manuscript should be edited to correct writing errors.
2- The Background in the abstract is similar to the Objective. In the Background, you should define the problem and the importance of the issue.
3- Abbreviations are confusing in the abstract.
4- HAART should be defined at first use.
5- Please define the inclusion and exclusion criteria for patient selection. Were patients with a possible diagnosis of cryptococcosis enrolled in the study?
6- Why did you not analyze the correlation between primary chest and CD4 count, as well as between dynamic changes in CT and HIV viral load? This should be mentioned in the discussion.
7- More literature review is recommended in the discussion to compare the consistency of the data with previously published works.

Editor-in-Chief

MAJOR REVISION 24 Jul 2022

Dear authors,
Your article needs Major Revision.
Regards

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Revision 3

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Dear Editors and Reviewers,

Thank you for your letter and for the reviewers' comments concerning our manuscript entitled "The correlation between CD4 cell count, HIV viral load and the chest CT findings in AIDS-associated pulmonary cryptococcosis". Those comments are all valuable and very helpful for improving our manuscript, as well as the important guiding significance to our researches. We have studied comments carefully and have made correction which we hope meet with approval. Revised portions are marked in red in paper. The main corrections in the paper and the responds to the reviewer's comments are as follows:

Reviewer 1:

1. Title and purpose: Based on the description of the method section and the results, the title and purpose of the study are not complete and appropriate and should be changed.

Answer:

The purpose of the study was rewritten in the abstract according to the Reviewer's comment (Page1, line 4-11), thank you so much.

2. Method Abstract: The method abstract section was written very briefly and incompletely; The method of grouping, ROC analysis and ICC should also be explained.

Answer:

Thank you for Reviewer's comment, we have modified the Method in the abstract and explained the method of grouping, ROC analysis and ICC which makes the abstract more clear (Page1, line 12-20).

3. Results: The presentation of the results is not in line the title and purpose of the study. It should not be expressed all results of tables in the text. Also, many of the results presented as text were not displayed in the tables.

Answer:

Based on the Reviewer's comment, we have revised the Results section, deleted some redundant content already mentioned in the table, and added the location and involvement of lung lesions to the *Table 1* (Page6, line 117-121; Page7,line 128.129; Page18, *Table 1*). Thank you so much for the comment.

4. The important point is that this study is longitudinal, but the results were presented cross-sectionally. The data should be displayed longitudinally and columns must be showed the values of CD4 and virus load at different times, and CT statues must be presented in the rows; and significant levels should be provided for both longitudinal and cross-sectional comparisons in the rows and columns

Answer:

In the part of the correlation study between CT morphology and viral load, the focus

was to compare the HIV viral load with different CT morphologies. According to the Reviewer's comment, we tried to put the CT morphology on the horizontal axis and the HIV viral load on the vertical axis, as shown in *Table* below. By comparing the original chart, the newly revised table may be a little bit more complicated and difficult to understand. Thank you very much for the comment, and we would like to try more different methods to show the results better.

Pulmonary lesions	Solid nodules				Cavitation					Consolidation infiltration
	solitary	multiple nodules	miliary nodules	Count	tiny cavity	Thin-walled cavity	Thick-walled cavity	Honeycomb cavity	Count	
Number	11	7	4	22	13	26	11	4	54	3
Percentage%	13.92	8.86	5.06	27.85	16.46	32.91	13.92	5.06	68.35	3.80
HIV-Viral load	61089±90070	129878±126583	731500±956697	204869±452464	217975±587537	170157±164315	451936±373602	254150±359408	245290±369272	29846±27798
p-value inner-group	&MN 0.721 &MIN 0.009	&SN 0.721 &MIN 0.024	&SN 0.009 &MN 0.024		&TNC 0.700 &TKC 0.122 &HC 0.862	&TC 0.700 &TKC 0.036 &HC 0.669	&TC 0.122 &TKC 0.036 &HC 0.356	&TC 0.862 &TNC 0.669 &TKC 0.356		
p-value inter-group		&C 0.932 &CI 0.588				&S 0.932 &CI 0.654				&S 0.588 &C 0.654[③]

5. Each word such as HAART must be written in full form for first time.

Answer:

We have checked all the acronyms and written in full form for first time , thanks to the Reviewer for their comments to make the article more standardized(Page1, line4-8,line 16.19; Page2, line 26; Page3, line36,38,39; Page4, line57,58,61).

6. All acronyms of tables must be described in bellow of them.

Answer:

All acronyms of tables have been described in bellow of them according to the Reviewer's comment, thanks to the comments to make the article more standardized

(Page18-19 Table 1; Page20, Table 2).

Reviewer 2:

Comment 1:
In line 8: The capital letter should not be used inside the sentence.
Answer:
Irregular use of acronyms in sentences has been revised, thanks to the comments to make the article more standardized (Page1, line9-10).

Comment 2:
In line 36: The crochet should be deleted.
Answer:
The crochet has been deleted, thank you so much for the comment (Page3, line46).

Comment 3:
In line 35 and 67: The phrase "solitary nodules" should be corrected. It seems the letter "s "must be deleted.
Answer:
The letter "s" has been deleted from the phrase "solitary nodules", thanks to the comment to make the article more standardized (Page5, line84).

Comment 4:
In line 78: It is reasonable to add a group which their radiological findings dose not change over time.
Answer:
We re-examined all enrolled patients in the section of the relation between CD4 cell counts increment and the change in lesion morphology and found that all enrolled patients had lesions' change whether in diameter or shape after 3-6 months' treatment. We would like to further collect cases after PC treatment, and if there are patients who meet the requirements, we would include them into the study. Thank you very much for the comment, it is very meaningful for us to do some related research.

Comment 5:
In line 70-72: According to which reference or literature, the cut off value and range of cavity wall thickness have been determined? The cavity with wall thickness more than 8 mm in which group is classified?
Answer:
According to references (8,9) inserted and based on the actual work, we made the cut-off value to distinguish thick-walled cavity and thin-walled cavity (Page5, line91-92). Thank you so much for the comment.
Reference 8: Watanabe Y, Kusumoto M, Yoshida A, Shiraishi K, Suzuki K, Watanabe SI, et al. Cavity Wall Thickness in Solitary Cavitary Lung Adenocarcinomas Is a Prognostic Indicator. Ann Thorac Surg. 2016;102(6):1863-71.

Reference 9: Zhou F, Ma W, Li W, Ni H, Gao G, Chen X, et al. Thick-wall cavity predicts worse progression-free survival in lung adenocarcinoma treated with first-line EGFR-TKIs. BMC Cancer. 2018;18(1):1033.

Comment 6:
In line 152 till 200: Discussion part has poor quality. It is expected that the main results of the study would mentioned in discussion part and compared with other similar studies. The literature review is weak in this article.
Answer:
According to the Reviewer's comment, we have revised the Discussion section, including adding the discussion of the main results and comparisons with previous related studies, while retaining the section about PC pathological changes reflecting the imaging changes and further explained the reason for choosing inspection time point. Thank you very much for your comment, this resulted in a great improvement in the quality of the manuscript (Page9, line168-Page12, line247).

Reviewer 3:

1- The manuscript should be edited in order of correct writing error
Answer:
The manuscript has been edited in order of correct writing error, thanks to the comment to make the article more standardized.

2- Background in abstract is similar to Objective, in background you should define the problem and the importance of issue
Answer:
Thank you so much for the Reviewer's comment, we have modified the Objective in the abstract and defined the problem the study trying to solved(Page1, line 8-12).

3- Abbreviations are confusing in abstract
Answer:
We have checked all the abbreviations and written in full form for first time both in abstract and Background in the article , thanks to the Reviewer for the comments to make the article more standardized(Page1, line12-16; Page2, line 25,27,34; Page3, line44,47,48; Page4, line65,66,69).

4- HAART should be define for the first time
Answer:
We have checked all the abbreviations and written in full form for first time both in abstract and Background in the article , thanks so much to the Reviewer' comment to make the manuscript more standardized(Page1, line4-8,line 16.19; Page2, line 26; Page3, line36,38,39; Page4, line57,58,61).

5- Please define the inclusion and exclusion criteria of patients selection, Does possible cryptococcosis diagnosis is enrolled in the study?

Answer:

According to the Reviewer's comment, we have added "1.3 Inclusion and exclusion criteria" in the Methods section and clarified the diagnostic criteria of the enrolled patients, that is, one of the definite diagnosis and the possible diagnosis can meet the diagnosis. Many thanks to the comment, this made the structure of the article clearer and easier to understand (Page4, line75-77; Page5, line78-81).

6- Why did not anlysis the correlation between primary chest and CD4 count, as well as dynamic changes in CT and HIV viral load? it should be mentioned in discussion

Answer:

The reason not to analyze the correlation between primary chest and CD4 count, as well as dynamic changes in CT and HIV viral load has been added to the Discussion part. Thank you very much for the questions. By explaining the above questions, I believe that the manuscript would become more comprehensive and reasonable (Page9, line180-187; Page10, line188-190).

7- More literature review is recommended in discussion to compare the consistency of data with previous published works

Answer:

According to the Reviewer’s comment, we have revised the Discussion section, including adding the discussion of the main results and comparisons with previous related studies, while retaining the section about PC pathological changes reflecting the imaging changes and further explained the reason for choosing inspection time point. Thank you very much for your comment, this resulted in a great improvement in the quality of the manuscript (Page9, line168-Page12, line247)..

We would like to express our great appreciation to you and reviewers for the valuable comments on our paper. We hope that the correction will meet with approval.

Looking forward to hearing from you.

Thank you very much.

Best wishes

Yours sincerely,
Ru-ming Xie

4 Revision 3

5 comments · 13 Aug 2022 – 7 Sep 2022

Referee 2 Reviewer — ACCEPT 13 Aug 2022

Currently, this manuscript has been appropriately revised and is ready for publication in the IJR from a methodological viewpoint.

Referee 3 Reviewer — ACCEPT 20 Aug 2022

Thank you for editing

Referee 1 Reviewer — ACCEPT 22 Aug 2022

The requested revision has been made.

Associate Editor — ACCEPT 31 Aug 2022

Dear authors
Thank you for considering the Iranian Journal of Radiology for your work. The manuscript could be accepted for publication.
Best regards

Editor-in-Chief — MINOR REVISION 7 Sep 2022

Dear authors,
Your article needs Minor Revision.
Regards

5

Revision 4

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Dear Editors and Reviewers,

Thank you for your letter and for the reviewers and editors' comments concerning our manuscript entitled "The correlation between CD4 cell count, HIV viral load and the chest CT findings in AIDS-associated pulmonary cryptococcosis". Those comments are all valuable and very helpful for improving our manuscript, as well as the important guiding significance to our researches. We have studied comments carefully and have made correction which we hope meet with approval. Revised portions are marked as highlighted lines/paragraphs. The main corrections in the paper and the responds to the editors and reviewers' comments are as follows:

Reviewers' Comments:

Reviewer 1:
Requested revision has been made.
Reviewer 2:
Thank you for editing.
Reviewer 3:
Currently, this manuscript appropriately revised and ready for publication in the IJR according to methodology view point.
Reviewer 4:
please write the data of SPSS manufacturer based on IBM site:
https://www.ibm.com/support/pages/how-cite-ibm-spss-statistics-or-earlier-versions-spss
References 6,7 are not cited in the text. Please cite them.

Answer:
Thank you for Reviewer's comment and the approval of the revised manuscript. We queried the data of SPSS manufacturer based on IBM site and modified it in the text (Page 6, line 111-112). Also, References 6 and 7 were highlighted in the text (Page 5, line 79). Thanks to the comment to make the article more standardized.

Associate Editor's Comments:

Associate Editor 1:
Thank you for considering the Iranian journal of radiology for your work. The manuscript could be accepted for publication.
Answer:
Thank you very much for your satisfaction with the revised manuscript. It's our pleasure to have the opportunity to be published in the *Iranian journal of radiology*.

Associate Editor 2:
1-please capitalize the first characters of words in title
Answer: The first characters of words in title were capitalized (Page 1, line 1.2).

Thank you very much for the comment.

2-in line 17, please delete curve before (ROC) and correct the part as: "receiver operator characteristic (ROC) curve"
Answer: The word 'curve' has been deleted (Page 1, line 17). Thanks to the comment to make the article more standardized.

3-the authors have written in line 19: "The intra-group consistency check (ICC)" while the ICC index that is used for assessment of reliability between observers is intra-class correlation coefficient. So I think, the authors mean "intra-class correlation coefficient" not "The intra-group consistency check". Please correct.
Answer: The phrase 'The intra-group consistency check (ICC)' has been modified (Page 1, line 19). Thank you for the comment.

4-please add full term off abbreviations in first time usage in abstract and paper separately. For example, in part (PMIN/SN=0.009; PMIN/MN=0.024) in abstract, PMIN/SN and PMIN/MN are unclear. [in addition: PTNC/TKC,
Answer: We have checked all the abbreviations and written in full form for first time both in abstract and Background in the article , thanks so much to the comment to make the manuscript more standardized (Page 1, line 21.22; Page 2, line 23.24).

5-this part is unclear: "improve and progress prognosis" do you mean better prognosis or improved prognosis or improve in prognosis? Please clarify.
Answer: The sentence has been rewritten (Page 2, line 25). Thank you very much for the comment.

6-please correct in abstract: "the sensitivity, the specificity and the accuracy were 0.815, 0.714 and 0.764, respectively."
Answer: The sentence has been rewritten according to the editor's comment (Page 2, line 28.29). Thank you for the comment.

7- the authors mentioned: "The cut-off value of CD4 cell count increment for differentiating …"I can not understand the meaning of increment here. Did you consider the increase of CD4 cell count or consider the number of CD4 cell count? Please explain and clarify.
Answer: Thank you for the comment. What we want to express was the 'increase of CD4 cell count', and the sentence has been rewritten (Page 2, line 26.27).

8-in line 29, HARRT is wrong. [HAART]. In line 80, please correct HAATR.
Answer: Due to our negligence, there was a mistake in the spelling of 'HAART', we have rechecked all the spelling of the manuscript (Page 2, line 31; Page 5, line 85; Page 8, line 161; Page 9, line 168; Page 10, line 199). Thank you so much for the comment.

9-objective part of abstract is unclear: "To observe the morphology of pulmonary lesions in Cryptococcus and the prognosis after HAART, the correlation between CT imaging features and HIV viral load, while the cut-off value of CD4 cell count increment for the prognosis was analyzed." [specially, the part after while …….] please rephrase.

Answer: According to the editor's comment, the objective part of abstract was rewritten (Page 1, line 9-11). Thanks so much to the comment to make the manuscript more standardized.

10-please add objective part to paper according to journal format.

11-please arrange titles as: 1-background, 2-objectives, 3-patients and methods, 3.1-patients, ….

Answer: According to the editor's comment, the objective part has been added to the paper and the subtitles were arranged (Page 3, line 51-56; Page 4, line 57.58.70; Page 5, line 80.87; Page 6, line 110; Page 7, line 123.124.140.). Thank you very much for the comment.

12-please write centre as center

Answer: The word was changed to 'center' (Page 4, line 61).

13-please correct >18 years to age greater than 18 years

Answer: The phrase was changed according to the editor's comment (Page 5, line 82).

14-please add full term of abbreviations in abstract and paper separately, for example, for PC in line 77, add full term

Answer: We have checked all the acronyms and written in full form for first time (Page 5, line 83) , thanks to the editor for the comment to make the article more standardized.

15-please correct: in line 76: Inclusion criteria were as follows. In line 78: Exclusion criteria were as follows

Answer: According to the editor's comment, the description has been modified (Page 5, line 81.83-84).

16-this part is somehow unclear. I recommend the authors to rephrase it: "In the improved group, nodules decreased, cavities became nodules and cavity walls became thinner were included, while in the progressed group, nodules enlarged and/or increased, nodules transformed into cavities, cavity walls became thicker and cases of infiltrations with ill-defined margin were observed."

Answer: Thank you for the comment. The sentence has been modified according to the comment (Page 6, line 101-105).

17-there is a sentence in lines 100-103 that is wrong [I think its verb should be made,

not making; line 101]. In addition, this sentence is long and I think it is better the authors rephrase it.
Answer: Thank you for the comment. The sentence has been *rephrased* according to the comment to make this part more clear to follow (Page 6, line 106-109).

18-please write the data of SPSS manufacturer better. [IBM Corp. is incomplete]. Please complete the data based on IBM site. [https://www.ibm.com/support/pages/how-cite-ibm-spss-statistics-or-earlier-versions-spss]
Answer: Thank you for the comment. We queried the data of SPSS manufacturer based on IBM site and modified it in the text (Page 6, line 111-112).

19-in line 106, do you mean as well as? Please consult an expert English editor for whole paper.
Answer: The phrase has been modified and checked of the paper according to the comment (Page 6, line 113). Thank you for the comment.

20-didn't you check the normality of data before statistical tests? Please add this point in statistical method section.
Answer: According to the comment of the editor, the statement for the normality of data was added (Page 6, line 113-114). Thanks so much to the comment to make the manuscript more standardized.

21-in line 110, the authors mentioned: "95% CI," but it is unclear for which variable did they calculate %95CI?
Answer: The sentence was modified to make it clear to follow (Page 6, line 118). Thank you for the comment.

22-please correct: " ….. 36.97±11. 91 years [range: 19–77]."
Answer: The phrase has been modified according to the comment (Page 7, line 130). Thank you for the comment.

23-this part is unclear: "The cases of all patients were complicated…."
24-this part is unclear: ".Among lesions distributed in less than 3 lobes, 29 patients (56.9%) was in lower lobe involvement"
Answer: Based on the Editor's comment, we have revised and checked the '4.1 Basic clinical characteristics and radiological features' part section and modified some sentences (Page 7, line 134.136.137). Thank you for the comment.

25-this part is not appropriate: "retroviral antiviral therapy." It could be written better as antiretroviral therapy.
Answer: The phrase has been modified according to the comment (Page 8, line 152). Thank you for the comment.

26-this part is unclear: "There was no statistically significant difference in the correlation between lesion morphology and HIV viral load in the three groups (S/CA p=0.932; S/C p=0.588; CA/C p=0.654)." it is unclear what is the meaning of sentence based on statistical point of view? Do you mean: "There were not statistically significant difference in HIV viral load between different subgroups determined based on lesion morphology [S vs. CA: P=0.932; ……]" in addition, it is recommended to correct this style in abstract too.
27-please correct: "MIN/SN" to "MIN vs. SN" and also MIN/MN to MIN vs. MN
Answer: Based on the Editor's comment, we have revised and checked the '4.2 Relation between chest CT findings and HIV viral load' part section and modified the writing style both in this part and in abstract (Page 8, line 152-154,156.157; Page 1, line 21.22, Page 2, line 23.24). Thank you for the comment.

28-if you used ANOVA for comparison of three groups, it is better to mention the post-hoc test used for pairwise comparisons of groups.
Answer: The Bonferroni Correction was used in ANOVA for the comparison of three groups, which was added to the '3.5 Data Analysis' part section (Page 6, line 116). Thank you so much for the comment.

29-in line 153 and 160 and 189, please correct HARRT
Answer: Due to our negligence, there was a mistake in the spelling of 'HAART', we have rechecked all the spelling of the manuscript (Page 2, line 31; Page 5, line 85; Page 8, line 161; Page 9, line 168; Page 10, line 199). Thank you so much for the comment.

30-in lines 154 and 156, it is better to write "were classified as"
Answer: The phrase has been modified according to the comment (Page 8, line 161.163.164). Thank you for the comment.

31-the authors mentioned: "After HARRT, 81.5% of lesions (54 lesions in 40 patients) were classified into the improved group, including 9 nodules decreased (16.7%), 7 cavity walls became thinner (12.9%) and 28 cavities turned to solid nodules (51.9%)." While 9+7+28=44 that is not equal to 54 and 40. Please correct. I think 54 should be 44.
Answer: Due to our negligence, there was a mistake in the numbers of lung lesions, we feel sorry about this, and we have rechecked all the number of the manuscript (Page 8, line 161). Thank you for the comment.

32-it is better the authors add P-Value for comparison of mean increase in CD4 cell count between improved vs. progressed groups.
Answer: The P-value for comparison of mean increase in CD4 cell count between improved vs. progressed groups has been added to the Result part (Page 9, line 171-173). Thank you for the comment

33-please correct: "95% CI=0.81-0.88; sensitivity, specificity and accuracy were 0.815, 0.714 and 0.764; respectively"
Answer: The sentence was modified according to the editor's comment (Page 9, line 174.175). Thank you for the comment.

34-the sentence in lines 181-184 is unclear. please rephrase.
Answer: The sentence was modified according to the editor's comment (Page 10, line 191-194). Thank you for the comment.

35-what is the meaning of "immune deficiency inner group"?
Answer: We have modified 'inner group' to 'within groups' to make it easy to understand (Page 11, line 213-214). Thank you for the comment.

36-this sentence is unclear: "Small focal areas of necrosis occur in some lesions after the necrotic material is eliminated through the bronchus when various types of cavity lesions form."
Answer: The sentence was modified according to the editor's comment (Page 11, line 228-230). Thanks to the comment to make the article more standardized.

37- References 6,7 are not cited in the text. Please cite them.
Answer: References 6 and 7 were highlighted in the text (Page 5, line 79). Thank you for the comment.

38-the percent (6.74) has no number in table 1.
Answer: Thank you very much for your detailed review, the number before the percent (6.74) has been filled in (Page 18, Table 1).

39-please explain in table 2 footnote about the writing style of E+04 or E+05 used in this table frequently.
*40-what is the meaning of inner in table 2? within group? please clarify [the better forms are between group and within group. it seems inter-group denotes to between group and inner group denotes within group. if you correct, please add this notification in footnote: *between group refers to comparisons between three groups of S, C and CA ** within group refers to comparisons between subgroups of patients determined in each main categories of solid, cavitation or consolidation]*
41-i think the style of [for example] TC/TNC could be better as TC vs. TNC. The authors could correct in table this style.
Answer: According to the editor's comments, we have revised Table 2, including explained the meaning of E+03 in the footnote of the table, revised and improved the definitions of 'within-group' and 'between groups', and revised the writing style of 'vs.' inside the table (Page 20, Table 2). Thank you very much for the comment to make the article more reasonable.

42-this part of figure 1 legend is unclear: "while sharp tiny nodules and GGO mixed

around the cavity (a).”
43-please correct in figure 2 legend: Fig.2A-C and capitalize the a, b and c
44-in figure 2 legend: In Review CT scan (c) …..
Answer: The Figure legends have been modified according to the editor’s comments. Thank you very much for the comment to make the article more standardized.

We would like to express our great appreciation to you and reviewers for the valuable comments on our paper. We hope that the correction will meet with approval.

Looking forward to hearing from you.

Thank you very much.

Best wishes

Yours sincerely,
Ru-ming Xie

5 Revision 4

1 comment · 18 Sep 2022

Editor-in-Chief

MINOR REVISION 18 Sep 2022

Dear authors,
Your article needs Minor Revision.
Regards

6

Revision 5

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Dear Editors,

Thank you for your letter and for the editor's comments concerning our manuscript entitled "The correlation between CD4 cell count, HIV viral load and the chest CT findings in AIDS-associated pulmonary cryptococcosis". Those comments are all valuable and very helpful for improving our manuscript, as well as the important guiding significance to our researches. We have studied comments carefully and have made correction which we hope meet with approval. Revised portions are marked as highlighted lines/paragraphs. The main corrections in the paper and the responds to the editor's comments are as follows:

Associate Editor 1:

1-in the objective part of abstract, this version seems better: [please carefully check the sentence to avoid conceptual mistake]

In this study, we are going to evaluate the correlation between CT features and HIV viral load, as well as the cut-off value of CD4 cell count increment in differentiating PC prognosis, the morphology of PC lesions and the prognosis after HAART.

Answer: According to the editor's comment, the objective part of abstract was rewritten (Page 1, line 8-11). Thank you so much for the comment to make the manuscript more standardized.

2-Definition of improved and progressed groups could be written better. I recommend one of the following versions [you can write the part based on your preference; these are recommendations]:

First version: Improved group included patients in whom the nodules decreased, cavities became nodules and cavity walls became thinner, while progressed group consisted the patients in whom nodules enlarged and/or increased, nodules transformed into cavities, cavity walls became thicker and patients with ill-defined margin infiltrations.

Second version: Improved group included patients in whom the nodules decreased or cavities became nodules or cavity walls became thinner, while progressed group consisted the patients in whom nodules enlarged and/or increased or nodules transformed into cavities or cavity walls became thicker or patients with ill-defined margin infiltrations.

3-considering my previous question, please note that above mentioned definitions of improved or progressed patients have an ambiguity: one cannot understand all of these criteria should be present in the patient at the same time to be included in improved or progressed groups or at least one of them suffices to consider the patient in the group? So I recommended two versions. Please clarify this point in the paper and choose the correct version.

Answer: Thank you so much for your recommendations. By comparing the two

versions, we prefer the second version to express the definition of the improved group and progressed group (Page 6, line 101-105). Meanwhile, we have clarified the conditions to be classified into the corresponding group (Page 6, line 105-106). Thanks again for the comment to make the manuscript more standardized and reduce ambiguity.

We would like to express our great appreciation to you for the valuable comments on our paper. We hope that the correction will meet with approval.

Looking forward to hearing from you.

Thank you very much.

Best wishes

Yours sincerely,
Ru-ming Xie

6 Revision 5

1 comment · 26 Sep 2022

Editor-in-Chief

ACCEPT 26 Sep 2022

Dear authors,
Your article is acceptable for publication in IJR.
Regards