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OPEN PEER REVIEW

Multidetector Computed Tomography Imaging Features of Inflammatory Myofibroblastic Tumors of the Gastrointestinal Tract in Adults: Radiological, Histopathological, and Immunohistochemical Features

In Young Choi, Suk Keu Yeom, Beom Jin Park, Deuk Jae Sung, Min Ju Kim, Na Yeon Han, Yang Shin Park, Sang Hoon Cha, So Yeon Kim, Jung-Woo Choi

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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 · 6 Aug 2022

Editor-in-Chief

MINOR REVISION 6 Aug 2022

Dear authors,
Before starting the review process for your article, it is necessary to clarify the following items:
- The link to your ethics code could not be found. Please replace it with an accessible link or upload the official approval document from your ethics committee.

- Please clarify the funding source and provide the grant number with a link or upload the official grant approval number.

- 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).

- The references you used are old. Please replace them with newer relevant references.
Regards

2

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.

No.: 129661

Title: MDCT Imaging Features of Inflammatory Myofibroblastic Tumor of the Gastrointestinal Tract in Adults: Comparison of Radiologic, Histopathologic, and Immunohistochemical Features

August 19, 2022

Editor-in-Chief

Iranian Journal of Radiology

-

Dear Editor-in-Chief

Thank you very much for allowing us to submit a revised manuscript addressing the reviewer ’s comments. Changes are highlighted in yellow in the revised version, and a point-by-point r eply to the reviewers is enclosed. We hope that the manuscript will now be considered suitabl e for publication in the Journal.

Sincerely,

Reply to the Reviewer:

We would like to thank the editor and the reviewers for the favorable review of our manuscri pt as well as the very helpful comments and constructive criticisms. Below are our point-by-point responses to the reviewers' comments.

1. *Please clarify the financial resource and mention the grant number with the link address or upload the official approval grant number.*
   → I am sorry for the problem with the link. I have attached a document from the IRB of our hospital.

2. *Please clarify the financial resource and mention the grant number with the link address or upload the official approval grant number.*

   → This research was supported by a Korea University Research Grant (K1925111). This grant is provided to support the research of the newly appointed full-time professor. This grant was received by the first author, IY.C, from Korea University. The research topic can be freely changed. I am sorry for not being able to attach the file. There is a limit to uploading up to two "other files" to this journal submission homepage.

3. *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 form exists in "conflict of interest" section of the site: https://brief.land/iranjradiol/knowledgebase/category/tree.html#conflicts_of_interest.html).*
   → Thanks for your kind explanation. The document was filled out and attached.

4. *The references you used are old. Please replace them with newer relevant references.*

   → We appreciate this comment. We replaced some old references with new references and added some new references.

5. In the process of re-submitting, the number of figure files was limited to 15. Originally, there were 19 figures in this paper, but figure 3 and figure 4c, which had relatively low importance, were deleted and related contents were modified.

2 Revision 1

4 comments · 13 Sep 2022 – 15 Oct 2022

Referee 1 Reviewer

MINOR REVISION 13 Sep 2022

Thanks to the authors for their submission to the IJR.
Firstly, it can be mentioned that the title of the study contains an interesting and rare outcome.
But it needs some revision as follows:
General
1. Since the sample size of the study is small, it should focus only on a descriptive objective. Therefore, these changes should be made in the title, objective, statistical analysis, and results presentation:
1.1. Title: The word comparison should be replaced with characteristics.
1.2. Objective: To be written as follows: "To describe characteristic of CT findings, pathologic specimens and histologic subtypes in adults with gastrointestinal IMTs ."
1.3. Statistical analysis: Analytical tests such as the Mann-Whitney U test and p-values should not be used, and the statistical analysis should be limited to descriptive indices such as the mean and standard deviation for normal quantitative data or the median and interquartile range (IQR) for non-normal quantitative variables, and the number and percentage for qualitative data.
1.4. Results presentation: The text and tables should be descriptive only, with no comparison between the two groups or reporting of significance levels.

Referee 2 Reviewer

MAJOR REVISION 27 Sep 2022

Thank you for submitting your valuable manuscript to the Iranian Journal of Radiology.
The main goal of this study was to assess the CT imaging features of inflammatory myofibroblastic tumors (IMTs) involving the gastrointestinal (GI) tract and compare these imaging characteristics with the different histopathologic subtypes. In this retrospective study, 11 patients with GI tract IMTs were enrolled. The authors concluded that, based on imaging, IMTs could be divided into two subtypes, a wall-thickening subtype and a well-circumscribed mass subtype, which correlate with specific histopathologic subtypes. In this regard, the myxoid-vascular pattern was mostly seen in the wall-thickening subtype, and the compact spindle cell pattern was commonly seen in the solitary mass-forming subtype.
The main strength of this study is its interesting subject, on which limited data are available in the literature. The manuscript is also well written.
The major limitation of the manuscript is the small sample size, although IMTs are rare, particularly when affecting the GI tract. In this manuscript, the authors discussed the histopathologic findings and immunohistochemistry results in detail, which might be boring for most radiologists. It was mentioned that two radiologists reviewed the CT imaging in consensus, a potential cause of bias.

MATERIALS AND METHODS:
Please clarify the exact definition of proximal bowel loop dilatation in lines 131-132.
The authors used the phrase ‘ peritumoral bowel wall thickening’ in line 133, which is not defined. It is also not clear how it is differentiated from the adjacent tumoral involvement.

DISCUSSION:
I would suggest rewriting the sentences in lines 252-254 in another way: In this study, most lesions showed a

low-density area in the central portion of the tumor, regardless of size or pathological pattern.
I recommend adding 'limitation' and ‘conclusion’ subsections separate from the ‘discussion’ part.

FIGURE AND LEGENDS:
Please add the names of the annotations used, such as white arrows or arrowheads, to the figure legends.

Associate Editor

MAJOR REVISION 14 Oct 2022

The manuscript was studied by three expert reviewers and by me, and I agree with them that it can be reconsidered after the reviewers’ suggested corrections have been made and their comments have been addressed.

Editor-in-Chief

MAJOR REVISION 15 Oct 2022

Dear authors,
Your article needs Major Revision.
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.

> **Reviewers' Comments:**

Reviewer 1:
Thank you for submission of your valuable manuscript to the Iranian journal of radiology.
The main goal of this study was to assess the CT imaging features of inflammatory myofibroblastic tumors (IMT) involving the gastrointestinal (GI) tract and compare these imaging characteristics with the different histopathologic subtypes. In this retrospective study, 11 patients with GI tract IMTs were enrolled. The authors concluded that based on imaging, IMTs could be divided into two subtypes, including wall-thickening and well-circumscribed mass which correlates with specific histopathologic subtypes. In this regard, the myxoid-vascular pattern was mostly seen in the wall-thickening subtype, and the compact spindle cell pattern was commonly seen in the solitary mass-forming subtype.
The main strength of this study is its interesting subject with limited data available in the literature. The manuscript is also well written.
The major limitation of the manuscript is the small sample volume, although IMTs are rare, particularly when affecting the GI tract. In this manuscript, the authors discussed the histopathologic findings and immunohistochemistry results in detail, which might be boring for most radiologists. It was mentioned that two radiologists reviewed the CT imaging in consensus, a potential cause of bias.

MATERIALS AND METHODS:
1. Please clarify the exact definition of proximal bowel loop dilatation in lines 131-132.
the authors used the phrase ‘ peritumoral bowel wall thickening’ in line 133, which is not defined. It is not also clear how it is differentiated from the adjacent tumoral involvement.

➔ Thank you for your kind comments. The imaging findings suggestive of bowel obstruction were clearly corrected according to the reference.

- Erik K Paulson, William M Thompson **Review of small-bowel obstruction: the diagnosis and when to worry** Radiology. 2015 May;275(2):332-42.

We used "peritumoral bowel wall thickening" as a term to express when the bowel wall around the tumor is thickened and the distinction from the tumor is not clear. The reason

for the thickening of the Bowel wall may be tumor involvement or reactive wall thickening due to inflammation. As you pointed out, we have corrected the term that may be confusing to another term, “concomitant thickening of peritumoral bowel wall”.

DISCUSSION:

2. I would suggest rewriting the sentences in lines 252-254 in another way: In this study, most lesions showed a low-density area in the central portion of the tumor, regardless of size or pathological pattern.

➔ Thank you very much for your kind correction. This sentence has been deleted because it was different from the result of this revision process.

3. I recommend adding the 'limitation' and ‘conclusion’ subsections separate from the ‘discussion’ part.

➔ As pointed out, limitations and conclusions are separated in the discussion.

FIGURE AND LEGENDS:

4. Please add the name of annotations used in the figure legends, such as white arrows or arrowheads.

➔ Thanks for your kind comment. We added descriptions for arrows and arrowheads to the figure legends.

Reviewer 2:

I have received the revised manuscript titled (MDCT Imaging Features of Inflammatory Myofibroblastic Tumor of the Gastrointestinal Tract in Adults: Comparison of Radiologic, Histopathologic, and Immunohistochemical Features).

Thanks for the detailed reply to the reviewers’ comments.

The title reflects the contents of the manuscript.

The abstract is complete and could be understood without reading the manuscript. No discrepancies exist between the Abstract and the remainder of the manuscript.

The manuscript is well written and there is no major English problem except a few spelling mistakes.

However, I would like to address some other concerns as follows:
1- You discussed about Lee et al study and mentioned: (They usually show a strong enhancement. This reported appearance is consistent with the results of our study of the IMT of the entire GI tract.) but earlier ,the imaging features of your cases were described as homogenous enhancement with iso to intermediate attenuation or peripherally enhancing solitary masses.

- ➔ Thanks for the good point. First of all, I apologize for the mistake in the sentence. "high- to iso attenuation" is correct, not "iso to intermediate attenuation". Most of the tumors in our study showed good enhancement. And since the cases are from multiple institutions, we could not measure the enhancement ratio or HU because the CT protocol of each case was different. Therefore, we consider the homogeneity of the tumor to be an important finding, and low-density lesions suspected of necrosis or hemorrhage inside the tumor. Most tumors in our study showed good enhancement, so we concluded that the results were consistent with previous studies. The expressions and results in Table 2, which may cause confusion, have also been corrected.

2- All the evaluated cases in your study were ALK negative. however when talking about ALK negative patients with older ages in Coffin et al study, you concluded: (it is considered that the number of cases of ALK positive patients was lower than the known frequency in our study) .please clarify your consideration.

- ➔ We thank the reviewer for your good and kind comments. Our study and Coffin's study had many differences in the study subjects. In Coffin's study, the 59 IMTs had an age at diagnosis ranging from 3 weeks to 74 years (mean 13.2 y, median 11 y), and the location of IMT was not limited to the gastrointestinal tract and included all IMT throughout the body. In their study, ALK-negative IMTs occurred in older patients

(mean age 20.1) years as compared with ALK-positive IMTs patients (mean age 13.2). IMT is more common in young people and rarer in old age.

In our study, we thought that the number of ALK-negative IMT patients would be small because many old adults were included. And these results are consistent with the findings of Coffin's study. As the reviewer pointed out, we have corrected the sentence because there may be misunderstandings in what we wrote.

3- Please correct the spelling of (mass- forming) in line 236.

➔ Thank you for your kind correction.

4- The arrows and arrowheads should be mentioned in the figure legends.

➔ Thanks for your kind comment. We added descriptions for arrows and arrowheads to the figure legend.

Reviewer 3:
Thanks to the authors for their submission to the IJR.
Firstly, it can be mentioned that the title of study contains an interesting and rare outcome.
But, it needs some revision as follows:
General
1. Since the sample size od study is small; it only should be focused on descriptive objective. Therefor, these editions should be done in the title, objective, statistical analysis, and results presentation:
1.1. Title: The word of comparison replaced by characteristics.
1.2. Objective: To be written as this manner "To describe characteristic of CT findings, pathologic specimens and histologic subtypes in adults with gastrointestinal IMTs ."

➔ Thank you for your kind and helpful comments. We also agree with your point. As pointed out, the title and purpose have been modified

1.3. Statistical analysis: Analytical tests like as Mann-Whitney U test and p-value shouldn't be used, and the statistical analysis should merely limited to the descriptive indices such as mean and standard deviation for normal quantitative data or median and intra-quartile range (IQR) for non-normal quantitative variables, and number and percentage for qualitative data.

➔ We apologize for our mistake. Thank you for your faithful comment. Due to the point of view, statistical comparisons were excluded from the text, and only the mean or median value was indicated.

1.4. Results presentation: The text and tables should be descriptive only, and made no comparison between two groups and expression of significance level.

➔ Thank you for your faithful comment. Statistical comparisons were excluded from the text and tables, and only the mean or median values were displayed.

3 Revision 2

3 comments · 6 Dec 2022 – 10 Dec 2022

Referee 1 Reviewer

MINOR REVISION 6 Dec 2022

Thanks to the authors for the appropriate revision of the manuscript. All comments have been addressed to some extent, but the following points must be considered:
1. According to my initial comment about the writing of the statistical analysis section, analytical tests such as the Mann-Whitney U test and p-values should not be used, and the statistical analysis should be limited to descriptive indices such as the mean and standard deviation (SD) for normal quantitative data or the median and interquartile range (IQR) for non-normal quantitative variables, and the number and percentage for qualitative data.
2. In all tables, it should be specified whether the numbers represent means, medians, counts, etc.

Associate Editor

MINOR REVISION 9 Dec 2022

The authors have made corrections and modifications. The revised manuscript still needs the minor revision suggested by one of the reviewers.

Editor-in-Chief

MINOR REVISION 10 Dec 2022

Dear authors,
Your article needs Minor Revision.
Regards

4

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.

Thank you very much for allowing us to submit a revised manuscript addressing the reviewer ’s comments. Additionally, I appreciate your nice words and warmth.
Changes are highlighted in yellow in the revised version, and a point-by-point reply to the rev iewers is enclosed. We hope that the manuscript will now be considered suitable for publicati on in the Journal.

> Reviewers' Comments:

Reviewer 1:
Thanks to the authors for appropriate revision of the manuscript. All comments relatively applied but following points must be considered:
1. According to my first time comment about writing of statistical analysis section; analytical tests like as Mann-Whitney U test and p-value should not be used, and the statistical analysis should merely limited to the descriptive indices such as mean and standard deviation (SD) for normal quantitative data or median and intra-quartile range (IQR) for non-normal quantitative variables, and number and percentage for qualitative data.

- ➔ Thank you very much for your kind correction. We apologize for our mistake. We corrected the statistical analysis section. We only used simple descriptive analysis and did not use the Maan-Whitney U test. As the reviewer pointed out, we recorded the mean and standard deviation for variables that follow a normal distribution and calculated the median for variables that do not. Because of the small number of variables, IQR was not recorded. The statistics professor at our hospital has reviewed these contents.

2. In all tables, it should be specified that the numbers are mean?, median?, count, ...

- ➔ Thank you for your kind comments. We corrected the tables by noting mean, median, and percentages.

4 Revision 3

3 comments · 3 Jan 2023 – 8 Jan 2023

Referee 1 Reviewer

ACCEPT 3 Jan 2023

Thanks to the authors for the final revision. Currently, it is acceptable for publication in IJR in terms of methodology.

Associate Editor

ACCEPT 4 Jan 2023

The revised manuscript can be accepted for publication.

Editor-in-Chief

MINOR REVISION 8 Jan 2023

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.

Thank you very much for allowing us to submit a revised manuscript addressing the reviewer ’s comments. We appreciate your kind and patient correction of our numerous errors. Changes are highlighted in yellow in the revised version, and a point-by-point reply to the rev iewers is enclosed. We hope that the manuscript will now be considered suitable for publicati on in the Journal.

1-please don’t use abbreviation in title

➔ MDCT, which was used as an abbreviation, was changed.

2-please change materials and methods to patients and methods. In addition, please change introduction to background.

➔ As you pointed out, I renamed the titles.

3-please add sequential numbers to titles and subtitles.

➔ We added sequential numbers.

➔ According to the instructions for authors of the Iranian journal of radiology, the limitation was not put in a separate subtitle in the Discussion section, and the conclusion was separated as a title.

4-in line 56, what is stoma? [stroma??]

➔ We apologize for our mistake, what you pointed out has been corrected.

5-is collgenized correct? [collagenized??]

➔ We apologize for our mistake, what you pointed out has been corrected.

6-please add objective part to the paper [before method section]

➔ We added the objective part.

7-what is the meaning of this part: “Each institutional review committee approved the experimental protocols.” This part does not make sense.

➔ Thank you for your kind comment, we corrected the sentence.

8-the authors mentioned they used three CT machines while the machines are two [Philips and GE]

➔ We apologize for our mistake, we corrected the sentence.

9-this part is unclear: “Other concomitant CT findings were evaluated in the presence or absence of bowel obstruction, peritumoral infiltration, peritumoral lymphadenopathy……”
[in fact, this point is unclear: in the presence or absence of bowel obstruction. Is assessment of findings dependent to bowel obstruction?]

➔ Thank you for your kind comment. In addition to the imaging findings of the tumor itself, we confirmed secondary peripheral findings, and the presence or absence of intestinal obstruction was one of them. We changed “in” to “, such as”.

10- this sentence is unclear, please re-write it: “The results were confirmed for an immunohistochemical study that can be reviewed including ALK, vimentin, SMA, CD34, desmin, cytokeratin, CD68, S-100, and C-kit.”

➔ We corrected the sentence.

11-please write SPSS manufacturer data based on the IBM site. [may be, SPSS ver. 20 is a product of IBM. Please check]

➔ We confirmed the manufacturer of our SPSS version.

12-in line 200, please correct homogenous to homogeneous.

➔ We apologize for our mistake, what you pointed out has been corrected.

13-in line 220, it seems the term immunochemical should be immunohistochemical.

➔ We apologize for our mistake, what you pointed out has been corrected.

14-in line 264, please correct: “…. older age and a higher ….”

➔ We apologize for our mistake, what you pointed out has been corrected.

15-in line 265, the part “IMTs patients” is better as “IMT patients”

➔ We apologize for our mistake, what you pointed out has been corrected.

16-it is better the authors add full term of abbreviations in first usage for example IgG

➔ Thank you for your kind comment. We used the full term for “IgG4” and “gastrointestinal” only at first, and changed the abbreviation afterwards.

17-what is the meaning of “intermediate biological potential” in line 280? Do you mean intermediate malignancy potential?

➔ Your point is correct. Malignancy has a clearer meaning. We changed it.

18-the authors wrote in limitation: ” The duration of follow-up ranged from 7 months to 7 years (mean 5 years). Therefore, we can rule out the possibility of late-onset metastasis after treatment.”
I think the second sentence should be written as: “Therefore, we can not rule out the possibility of late-onset metastasis after treatment.” Please check.

➔ We apologize for our mistake, what you pointed out has been corrected.

19-in table 1, the word Medication is better to be replaced with medical therapy

➔ We corrected the word.

20-in table 1, please correct: Follow up period (days) 1827.2 ± 1776.6.

➔ Thank you for your point out, we corrected it.

21-in table 2, please correct Homogeneous and heterogeneous

➔ We apologize for our mistake, what you pointed out has been corrected.

22-in table 2, please correct: Intussusception

➔ We apologize for our mistake, what you pointed out has been corrected.

23-in figure 2 legend, please correct aroow.

➔ We apologize for our mistake, what you pointed out has been corrected.

24-this part is unclear in figure 3 legend: “…. with confirmed loosely arranged type in the ileum.”

➔ We corrected the sentence.

25-in figure 4 legend, “becomes contrast enhancement” seems wrong. Better version seems to be: “becomes contrast enhanced”. Please get advice from editor.

➔ We corrected the sentence.

26-Figure 4e is a Contrast-enhanced T1-weighted image but you mentioned it as T2-weighted image. Please correct the legend.

➔ We apologize for our mistake, we corrected the issue.

5 Revision 4

1 comment · 14 Jan 2023

Editor-in-Chief

ACCEPT 14 Jan 2023

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