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The misclassification of gastric antral vascular ectasia

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The Misclassification of Gastric Antral Vascular Ectasia
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Dear Dr. Aryan,

Reviewers have now commented on your paper. You will see that they are advising that you revise your manuscript. If you are prepared to undertake the work required, I would be pleased to reconsider my decision.

For your guidance, reviewers' comments are appended below.

If you decide to revise the work, please submit a list of changes or a rebuttal against each point which is being raised when you submit the revised manuscript. Also, please ensure that the track changes function is switched on when implementing the revisions. This enables the reviewers to rapidly verify all changes made.

Your revision is due by May 29, 2022.

To submit a revision, go to https://www.editorialmanager.com/jctres/ and log in as an Author. You will see a menu item call Submission Needing Revision. You will find your submission record there.

Yours sincerely

Michal Heger
Editor-in-Chief
Journal of Clinical and Translational Research

Reviewers' comments:

Reviewer #1: 1. In the topic its mentioned Misclassification while in the text, it is mostly discussed as misdiagnosis. Please clarify and define (a) Define Misclassification (b) is misclassification and misdiagnosis same
2. Need to clarify more the term misdiagnosis: (a) does it mean that diagnosis was actually GAVE but misdiagnosed as some other terminology like erythema, ulcer etc OR it's also applicable to vice versa (eg.it was actually erythema but labelled as GAVE)
3. Re-classification was lacking - please clear this point.
4. No of patients mentioned 110 total with the diagnosis of GAVE. However if we add the number of patients diagnosed GAVE with different conditions mentioned like cirrhosis (90) , CKD (28) and (13) with ESRD on hemodialysis. This reflect that this number is more than 110 ie 131. So you can mention
also the GAVE patients having more than 1 conditions from above list.
5. In table 3 patients who were labeled GAVE on endoscopy and were biopsied also was 58. 15 out of these was labeled negative for GAVE on biopsy while 43 were positive for GAVE on biopsy. So to apply this on the patients who were labelled endoscopic ally GAVE but didn't go for biopsy, there is expected about 25% of cases of these to be GAVE negative if it would have been biopsied. Is this taken in to account in data/statistics and in discussion?
6. GAVE SCORE description?
7. Was there any patient who was labelled normal EGD and later diagnosed as GAVE if yes could it be due to main factor of air insufflation during EGD. it's rarely observed that if you put more air in stomach then GAVE lesion might disappear (we diagnosed one case on capsule endoscopy as it was normal EGD and then re-scoped with less air insufflation) . so in recommendations in addition to more emphasis for trainee one can add this factor of putting less air insufflation if you highly suspect suspect GAVE.
8. Need prospective study with GAVE findings and biopsy for all patients.

Authors' response

To the Editorial Board,

We very much appreciate the opportunity to submit our manuscript to *Journal of Clinical and Translational Research.* We are very grateful for the time the reviewers took into reading and critiquing our manuscript. We have responded to each reviewer's comment on a point-by-point basis and made the appropriate changes to the manuscript. We hope you find the changes appropriate and hope to hear back soon.

Thank you,

Mahmoud Aryan

Reviewer #1:

1. In the topic its mentioned Misclassification while in the text, it is mostly discussed as misdiagnosis. Please clarify and define (a) Define Misclassification (b) is misclassification and misdiagnosis same
    a. Thank you for the comment. Misclassification and misdiagnosis were used synonymously throughout the text. Misclassification and misdiagnosis were defined as labeling these lesions as other entities (erythema, gastritis, polyps, etc) despite these lesions actually representing GAVE. The application of the term misclassification is more appropriate for visual EGD finding, whereas misdiagnosis is more applicable for pathology findings. We therefore use both terms, but they are synonymous with regards to their overall definition. This was further clarified and edited in the text.

2. Need to clarify more the term misdiagnosis: (a) does it mean that diagnosis was actually GAVE but misdiagnosed as some other terminology like erythema, ulcer etc OR it's also applicable to vice versa (eg.it was actually erythema but labelled as GAVE)
    a. Thank you for the comment. Misclassification and misdiagnosis were defined as labeling culprit lesions as other entities (erythema, gastritis, polyps, etc) despite these lesions actually representing GAVE. This was added to the text.

3. Re-classification was lacking - please clear this point.

    a. Thank you for the comment. We highlighted the fact that GAVE is frequently missed during endoscopic evaluation and described in other terms like erythema or gastritis. These lesions are later on reclassified as GAVE after multiple EGD procedures. The final proper diagnosis of GAVE was verified by two separate board-certified Gastroenterologists/Hepatologists after reclassification of all the EGD findings. This was added to our manuscript.

4. No of patients mentioned 110 total with the diagnosis of GAVE. However if we add the number of patients diagnosed GAVE with different conditions mentioned like cirrhosis (90) , CKD (28) and (13) with ESRD on hemodialysis. This reflect that this number is more than 110 ie 131. So you can mention also the GAVE patients having more than 1 conditions from above list.
    a. Thank you for the comment. We will specify in the text that some patients had more than one co-morbidity. There were 28 patients with both CKD and cirrhosis, while there were 11 patients with both ESRD and cirrhosis. This was added to the text.

5. In table 3 patients who were labeled GAVE on endoscopy and were biopsied also was 58. 15 out of these was labeled negative for GAVE on biopsy while 43 were positive for GAVE on biopsy. So to apply this on the patients who were labelled endoscopic ally GAVE but didn't go for biopsy, there is expected about 25% of cases of these to be GAVE negative if it would have been biopsied. Is this taken in to account in data/statistics and in discussion?
    a. Thank you for the comment and we agree with the comment. We point out in our discuss that biopsy has a high false negative rate in GAVE. Therefore, amongst the 65 cases that were not classified as GAVE on initial EGD while

also not receiving a biopsy, it would have been expected that some of these lesions return negative for GAVE if they had been biopsied given the patchy nature of the disease and the high false negative rate. This was further clarified in the test.

6. GAVE SCORE description?
    a. Thank you for the comment. The GAVE score has 3 criteria and is a 5-point score. Fibrin thrombi and/or vascular ectasia are the first criteria for which 1 point is given to only one being present, and 2 points is given to both being present. Spindle cell proliferation is the second criterion for which 1 point is given for increased proliferation and 2 points is given for marked increased proliferation. The third criterion is fibrohyalinosis where 1 point is given for the presence of fibrohyalinosis. A GAVE score ≥3 has been deemed to be the best indicator of GAVE on biopsy. This was added to the text.

7. Was there any patient who was labelled normal EGD and later diagnosed as GAVE if yes could it be due to main factor of air insufflation during EGD. it's rarely observed that if you put more air in stomach then GAVE lesion might disappear (we diagnosed one case on capsule endoscopy as it was normal EGD and then re-scoped with less air insufflation) . so in recommendations in addition to more emphasis for trainee one can add this factor of putting less air insufflation if you highly suspect suspect GAVE.

    a. Thank you for the comment. Any maneuvers geared towards clear visualization of the antrum will aid in the visual diagnosis of GAVE. It is important that the ideal amount of air insufflation is applied to prevent either over insufflation or under insufflation to therefore achieve clear view of the antrum and the remainder of the stomach.[19]

8. Need prospective study with GAVE findings and biopsy for all patients.

    a. Thank you for the comment. We agree with the comment. We started designing a prospective study with an IRB pending to study the histopathology and clinical features of GAVE. We are working on making a template available in the system we use for documentation of endoscopic procedures. This will hopefully make it easier for the endoscopist to document the location and description of GAVE.

2nd Editorial decision

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Dear authors,

I am pleased to inform you that your manuscript has been accepted for publication in the Journal of Clinical and Translational Research.

You will receive the proofs of your article shortly, which we kindly ask you to thoroughly review for any errors.

Thank you for submitting your work to JCTR.

Kindest regards,

Michal Heger
Editor-in-Chief
Journal of Clinical and Translational Research

Comments from the editors and reviewers: