

Tagging incidental finding of fatty liver on ultrasound: A novel intervention to improve early detection of liver fibrosis

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Review timeline:

Received: 7 December, 2020
Editorial decision: 12 August, 2021
Revision received: 8 September, 2021
Editorial decision: 9 September, 2021
Published online: 29 September, 2021

1st Editorial decision

12-Aug-2021

Ref.: Ms. No. JCTRes-D-20-00146

Tagging incidental finding of fatty liver on ultrasound: A novel intervention to improve early detection of liver fibrosis

Journal of Clinical and Translational Research

Dear Dr. Nagra,

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 Sep 11, 2021.

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 #2: The manuscript titled "Tagging incidental finding of fatty liver on ultrasound: A novel intervention to improve early detection of liver fibrosis" was reviewed.

This is a single center retrospective study evaluating "tagging" of radiology reports by means of inserting a recommendation statement to radiology reports. The use of the word "novel" is misleading. A recommendation in a radiology report is not a novel intervention. It is a traditional practice in radiology reporting! I suggest the use of this word is revisited or perhaps omitted!

Further comments below.

Abstract

Severe / advanced fibrosis is stage 3 or 4 while significant fibrosis includes stage 2 (\geq stage 2 fibrosis).

Please correct this here and the rest of the manuscript, abstract, tables and figures.

When using abbreviations such as BMI, the complete wording should be used first in the manuscript when it is first encountered e.g. body mass index (BMI). Please correct this throughout the manuscript and for any other abbreviation.

Background section of abstract requires editing and re wording

Terms such as "In our health care system" and "we often see" are redundant.

This statement "Acknowledging incidental finding of fatty liver on abdominal imaging and identifying patients at risk of having advanced liver fibrosis helps in preventing its progression to cirrhosis." is not entirely true. Acknowledging ... may help in preventing

Page 4

Line 52

... on abdominal imaging. The word "imaging" should be replaced with "ultrasound"

Line 52 to 57

When steatosis is identified, there aren't clear guidelines on which patients may have a higher risk of having NASH and which patients would benefit from further clinical evaluation.

This statement is not accurate. There are guidelines and recommendations on how to assess patients with fatty liver detected incidentally.

Line 57 to 60

Currently, we do not have reliable non-invasive testing to stratify these cases, and liver biopsy is required to truly differentiate NASH from benign steatosis.8

This statement is not correct. Magnetic resonance elastography is a reliable non-invasive test to assess fibrosis in patients with fatty liver. However, this is an expensive modality which is not widely available. Biopsy can be considered but the invasive nature precludes its routine use.

Also consider using a more recent reference. Reference 8 is from 1997!

Page 5

Statement ending in line 7. Please add a reference
Statement ending in line 24, Please add a reference

Page 6

Line 41

Hence mean time of review

Is it "minimum" time of review instead of "mean"? given the review was till Aug 2019 and the study period ended in Sept 2017

Page 7

Line 9 to 12

"For this study, normal alanine transaminase (ALT) was defined as < 35 U/L for men and < 25 U/L for women."

Please provide a reference article(s) for these values or clarify that these thresholds are used in your own center's lab for normal range.

Line 39

Advanced fibrosis is stage 3 or 4 not d (\geq stage 2) fibrosis

Please correct this here and the rest of manuscript and abstract

Page 8

Please give interquartile range with median age then number and % of women:
Median age of patients was 54 years (IQR, xx to xx), and zz (53.2%) were women.

"In terms of body mass, 9.7% had BMI < 25, 28.9 % had BMI 25-30, 31.8 % had a BMI 30-35, 13.9% had BMI 35-40, and 15.4% had BMI of > 40."

For categories, there should be no overlap in the values. For example 25.0 - 29.9, 30.0 - 34.9 and so forth

Please correct this in the text and Tables

"Patients with DMII were also not more likely to be referred, and in fact a lower percent of those with diabetes (19.7 vs 24.9%) were seen in hepatology clinic."

Was this significant? Please include P value if significant

Page 9

Line 36

"stage 2 fibrosis" please use F2 for consistency when referring to stage 2 fibrosis similar to the rest of manuscript

Also please clarify significant fibrosis from severe / advanced fibrosis. See initial comment regarding this.

Figure 1.

Clarify significant fibrosis from severe / advanced fibrosis

Page 17

Discussion, second paragraph

Line 42

...natural history of fatty liver disease, up to 75-80% of these cases are likely benign."

Please include reference for this statement

Page 18

First paragraph should also mention ultrasound shearwave elastography in addition to FibroScan and MRE

Page 20

Line 22

No need to report P value or refer to Figures in the Discussion part of a paper

Page 21

One of the limitations mentions "white" ethnicity as the majority of the cohort. This was not referred to in the methods or results. If ethnicity is available as a variable for the study, results on this variable should be presented. If it is not available for analysis, it should be stated in the methods section with a statement that the predominant ethnicity in the cohort is white.

Page 22

The last two sentences in the discussion part are redundant. Please re word the conclusion or remove those sentences.

Authors' response

Dear reviewers,

Thank you so much for your feedback.

We have thoroughly reviewed and revised our manuscript as per your suggestions/comments. We have responded to each suggestion as below.

Please let us know if they are any further questions/concerns.

Sincerely,

Navroop Nagra

1.Reviewer #2: The manuscript titled "Tagging incidental finding of fatty liver on ultrasound: A novel intervention to improve early detection of liver fibrosis" was reviewed.

This is a single center retrospective study evaluating "tagging" of radiology reports by means of inserting a recommendation statement to radiology reports. The use of the word "novel" is misleading. A recommendation in a radiology report is not a novel intervention. It is a traditional practice in radiology reporting! I suggest the use of this word is revisited or perhaps omitted!

Response:

We consider a radiology impression that has a specific recommendation to consult hepatology for new diagnosis of fatty liver as novel, given we know from our own data and other studies that the finding of steatosis, when buried in the findings, often goes ignored. This is not standard clinical practice, and hence we do feel this is a novel and unique intervention. Traditionally radiologists recommend further or alternative imaging but recommendation to consult a sub-speciality (hepatology) is a unique intervention in radiology report.

Abstract

2 .Severe / advanced fibrosis is stage 3 or 4 while significant fibrosis includes stage 2 (\geq stage 2 fibrosis).

Please correct this here and the rest of the manuscript, abstract, tables and figures.

Response – We have corrected this in the entire manuscript and the abstract.

3. When using abbreviations such as BMI, the complete wording should be used first in the manuscript when it is first encountered e.g. body mass index (BMI). Please correct this throughout the manuscript and for any other abbreviation.

Response – We have corrected this in the entire manuscript and checked for other abbreviations as well.

4. Background section of abstract requires editing and re wording

Terms such as "In our health care system" and "we often see" are redundant.

This statement "Acknowledging incidental finding of fatty liver on abdominal imaging and

identifying patients at risk of having advanced liver fibrosis helps in preventing its progression to cirrhosis." is not entirely true. Acknowledging ... may help in preventing

Response – We have omitted these words and rephrased the entire paragraph.

5. Page 4

Line 52

... on abdominal imaging. The word "imaging" should be replaced with "ultrasound"

Response - We have replaced the word as suggested.

6. Line 52 to 57

When steatosis is identified, there aren't clear guidelines on which patients may have a higher risk of having NASH and which patients would benefit from further clinical evaluation.

This statement is not accurate. There are guidelines and recommendations on how to assess patients with fatty liver detected incidentally.

Response – We have corrected this and rephrased most of the paragraph.

7. Line 57 to 60

Currently, we do not have reliable non-invasive testing to stratify these cases, and liver biopsy is required to truly differentiate NASH from benign steatosis.⁸

This statement is not correct. Magnetic resonance elastography is a reliable non-invasive test to assess fibrosis in patients with fatty liver. However, this is an expensive modality which is not widely available. Biopsy can be considered but the invasive nature precludes its routine use.

Response- Since NASH by definition is a histopathological diagnosis therefore biopsy is needed to truly differentiate NASH from NAFLD. However, if we rule out other secondary causes of hepatic steatosis then we can assess degree of fibrosis by MRE/fibroscan/Shearwave elastography and if fibrosis is present then we can attribute it to NASH. We have rephrased the entire paragraph as per your suggestions, new references are also added in addition to the old reference.

8. Also consider using a more recent reference. Reference 8 is from 1997!

Response – New reference added in addition to the old reference.

9. Page 5

Statement ending in line 7. Please add a reference
Statement ending in line 24, Please add a reference

Response – We have added the references.

10. Page 6

Line 41

Hence mean time of review

Is it "minimum" time of review instead of "mean"? given the review was till Aug 2019 and the study period ended in Sept 2017

Response: Agree, revised in manuscript

11. Page 7

Line 9 to 12

"For this study, normal alanine transaminase (ALT) was defined as < 35 U/L for men and < 25 U/L for women."

Please provide a reference article(s) for these values or clarify that these thresholds are used in your own center's lab for normal range.

Response – We used these values as per our hospital's lab normal range, which is consistent with ACG guidelines published in 2017. We added reference and edited text.

12. Line 39

Advanced fibrosis is stage 3 or 4 not d (\geq stage 2) fibrosis

Please correct this here and the rest of manuscript and abstract

Response – We have corrected this in the entire manuscript and the abstract.

13. Page 8

Please give interquartile range with median age then number and % of women:

Median age of patients was 54 years (IQR, xx to xx), and zz (53.2%) were women.

Response – We have added these numbers.

14. "In terms of body mass, 9.7% had BMI < 25, 28.9 % had BMI 25-30, 31.8 % had a BMI 30-35, 13.9% had BMI 35-40, and 15.4% had BMI of > 40."

For categories, there should be no overlap in the values. For example 25.0 - 29.9, 30.0 - 34.9 and so forth

Please correct this in the text and Tables

Response- We have corrected this as suggested

15. "Patients with DMII were also not more likely to be referred, and in fact a lower percent

of those with diabetes (19.7 vs 24.9%) were seen in hepatology clinic."
Was this significant? Please include P value if significant

Response – It was not significant and we have added P value as suggested.

16. Page 9

Line 36

"stage 2 fibrosis" please use F2 for consistency when referring to stage 2 fibrosis similar to the rest of manuscript

Also please clarify significant fibrosis from severe / advanced fibrosis. See initial comment regarding this.

Response- Dear reviewers, we have corrected this in the entire manuscript and have also clarified significant fibrosis (\geq F2) vs advanced fibrosis (F3/F4)

17. Figure 1.

Clarify significant fibrosis from severe / advanced fibrosis

Response – We have clarified this.

18. Page 17

Discussion, second paragraph

Line 42

...natural history of fatty liver disease, up to 75-80% of these cases are likely benign."

Please include reference for this statement

Response – We have added the reference.

19. Page 18

First paragraph should also mention ultrasound shearwave elastography in addition to FibroScan and MRE

Response – We have added this as suggested

20. Page 20

Line 22

No need to report P value or refer to Figures in the Discussion part of a paper

Response – We have corrected this.

21. Page 21

One of the limitations mentions "white" ethnicity as the majority of the cohort. This was not referred to in the methods or results. If ethnicity is available as a variable for the study, results on this variable should be presented. If it is not available for analysis, it should be stated in the methods section with a statement that the predominant ethnicity in the cohort is white.

Response – We have corrected this and reported about predominant ethnicity being white in the methods section as suggested.

22. Page 22

The last two sentences in the discussion part are redundant. Please re word the conclusion or remove those sentences.

Response- We have removed the last two lines as suggested

2nd Editorial decision
09-Sept-2021

Ref.: Ms. No. JCTRes-D-20-00146R1
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Journal of Clinical and Translational Research

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: