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OPEN PEER REVIEW

Monocyte-to-High-Density Lipoprotein Ratio may be Related to the Coronary Artery Disease Reporting and Data System Score and Increased Left Ventricular Mass

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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

5 comments · 9 Sep 2021 – 25 Sep 2021

Referee 1 Reviewer

MAJOR REVISION 9 Sep 2021

Thanks to the authors for submitting their manuscript to the IJR.
Overall, it can be said that the title of the study is important and interesting; however, the following methodological points are concerning:
1. Inappropriate study design: It is best to design a cohort study, or it is better to apply a case-control approach, but a cross-sectional method has been used here.
2. Small sample size: There are similar works with larger sample sizes.

Referee 2 Reviewer

MAJOR REVISION 18 Sep 2021

The submitted manuscript investigated the possible relationship between the coronary artery disease severity scoring system (CAD-RADS), the monocyte-to-HDL ratio, and the left ventricular myocardial mass.
The major concerns are as follows:
1- A few minor spelling and grammatical errors need to be rectified.
2- It is not mentioned whether any patients were taking antihypertensive or antidiabetic medications.
3- Did the authors have any CAD-RADS 5 (Total occlusion) cases? While there are data regarding the CAD-RADS 5 cases in the first paragraph of the Discussion section, no information is provided in the tables.
4- Please state whether there were any coronary vulnerable plaques in your cases. If so, please provide the data on the monocyte count and HDL measurements in these patients.
5- The protocols and techniques of CT data acquisition (kVp, mAs, Collimation, ...) have to be mentioned in detail.
6- It is recommended that the city and country of the CT machine manufacturer be stated.
7- Please provide information about the viewing workstation and the viewing software (e.g., Syngo Via version?).
8- How many years of experience in coronary CTA interpretation does the radiologist have? Please specify.
9- The ethics committee approval number is missing in the main text, although it is included in the Abstract.
10- Did the authors correlate the findings and results with Syntax Score as well? Please clarify.
11- In Table-1, the interpretations of CAD-RADS 3 and CAD-RADS 4 as Moderate Stenosis and Severe Stenosis, respectively, are missing. Moreover, CAD-RADS 5 as Total Occlusion is not mentioned.

Referee 3 Reviewer

MAJOR REVISION 21 Sep 2021

Dear authors,
Regarding the manuscript “Monocyte to HDL Ratio may Relate to CAD-RADS Score and Left Ventricular Mass”, I have the following comments:
- The writing structure of the text is complex, which makes it difficult to understand what the authors mean.
- In section 2.3, I didn’t understand how you calculated LVM. Would you please clarify the equation?
- In section 2.5, the approval number is not noted.
- In the discussion section, it was noted that MHR can be a marker for the early diagnosis of atherosclerosis. But it should be mentioned that the submitted study doesn’t necessarily lead to this conclusion, and it can only be considered a risk factor for atherosclerosis.

- Since LVM is related to HTN and, on the other hand, coronary artery disease is related to HTN, it cannot be concluded that CAD is related to LVM unless hypertension is considered the primary factor. How did you conclude that LVM is an independent risk factor for CAD? The same problem also applies to the relationship between MHR and LVM.

Associate Editor

MAJOR REVISION 25 Sep 2021

Based on the reviews, the submitted manuscript requires MAJOR REVISION before it can be reassessed.

Editor-in-Chief

MAJOR REVISION 25 Sep 2021

Dear authors,
Your article needs Major Revision.
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.

Dear Editor,

Thank you for your letter and for the reviewers’ comments concerning our manuscript. Those comments are all valuable and helpful for improving our work. We have studied these comments carefully and have made corrections that we hope will meet with your approval. The revised components are marked in yellow in the manuscript. The main corrections to the manuscript and the responses to the reviewers’ comments are listed below.

Reviewers' Comments:

Answers to Reviewer 1.

1. “-The writing structure of the text is complex which makes it difficult to understand the authors' means”

   The complex writing structure of the text language was arranged to be more understandable and simple.

2. “- In section 2.3, I didn’t understand how did you calculate the LVM. Would you please clarify the equation?”

   The measurement method of LVM is explained in detail under subtitle 2.1. The CT device automatically calculates the LVM value based on this method.

3. “ - In the 2.5 section the approval number is not noted. “

   Approval number added to the text 2021/3180

4. “- In the discussion section, it was noted that the MHR can be a marker for early diagnosis of atherosclerosis. But it should be mentioned that the submitted study doesn’t necessarily lead to this conclusion, and it can only be noticed as a risk factor for atherosclerosis.”

   We agree with your valuable suggestion. We changed this section as follows.

   We found a relation between MHR and CAD-RADS score and determined the cutoff values for this score. Our study cannot reveal that MHR is a definitive marker for CAD-RADS. However, it can display that MHR may be an inexpensive and reliable predictive marker for CAD-RADS scoring. The current study may reveal that MHR is only a risk factor for atherosclerosis.

5. “- Since LVM is related to HTN and on the other hand, coronary artery disease is related to HTN, it cannot be concluded that CAD is related to LVM unless hypertension is noticed as the primary factor. How did you conclude the LVM as an independent risk factor for CAD? The same problem is also true with the relation between MHR and LVM.”

   We agree with your valuable suggestion. We changed this section as follows.

   There was a relationship between LVM and CAD-RADS scores in univariate analysis, but we could not find an association with multivariate analysis. Unless hypertension is recognized as the primary factor for CAD, it cannot be concluded that CAD is associated with LVM. Our findings may suggest that MHR may be a marker for CAD-RADS score, but not LVM.

Answers to Reviewer 2.

1. Please describe the demographic data of all of the patients enrolled in the study.

Demographic data of all patients included in the study are summarized in table 2.

2. What was the indication for the use of coronary CT angiography in the patients? Was it due to stable coronary artery disease or for ruling out acute coronary disease?

CCTA was performed to rule out significant luminal stenosis in stable patients with suspected coronary stenosis. Added as an expression to the method section.

3. Please specify the software used for the evaluation of coronary CT angiography in the current study.

Coronary computed tomography angiography imaging was performed using a Somatom Drive 2x128 Dual Source CT scanner (Siemens Healthineers, Erlangen, Germany). All Image data were evaluated with CT Cardiac Function clinical software application on Syngo Via (version VB 20A) Workstation (Siemens Healthineers, Erlangen, 2019, Germany.

And detailed information about CT device and used post process evaluation explained in the text. And detailed information about CT device and used post process evaluation explained in the text.

4. While you mentioned that LV mass was calculated via dedicated software, please describe more about the method of calculating LV mass.

Our new generation coronary CT device can automatically calculate the LVM value. The measurement technique of LVM is mentioned in detail in the 2.1 subtitle.

5. In table 1, I think CAD-RADS 3 and 4 should be interpreted as moderate and severe stenosis, respectively.

The corrections you specified have been applied to the table.

6. in table 2, please specify the units used for EF, SV, Esv, Edv, and CO.

The units as you stated have been applied to the text.

7- Although you mentioned the limitations of the current study which were relatively small population and being a single-center study, in my view it is better to conclude more conservatively in the discussion section about your results.

Our study is a pilot study in this field. Multicenter and prospective studies are needed on this subject. As you mentioned; in the discussion and conclusion sections, regulations showing a conservative approach were made.

8- Regarding submitting the current manuscript in a radiology journal, adding a few images, including the use of dedicated software for calculating LV mass, could be helpful.

We added images to the text. About LVM and vulnerable plaque.

Answers to Reviewer 3:

1. A few minor dictation and grammatical errors exist, to be rectified.

The article was re-evaluated in terms of grammatical errors.

2. It is not mentioned if any patient(s) was (were) taking anti-hypertensive or anti-diabetic medications.

The drug use information of the patients was added to the method section as follows.

All patients with hypertension included in the study were using anti-hypertensive drugs, and all patients with diabetes included in the study were using anti-diabetic drugs.
4. Did the authors have any CAD-RADS 5 (Total occlusion) case(s)? While there are data regarding the cases of CAD-RADS 5 in the first paragraph of the Discussion section.

No CAD-RADS-5 lesion was not detected in any of our patients. Added as information to the method section.
5. Please state if there was any coronary vulnerable plaque in your cases. If so, please provide the data to demonstrate the monocyte count and HDL measurements in these patients.

First of all, I would like to thank you for pointing out this subject, which we think adds a different value to the study. By re-evaluating the CCTA images of all patients included in the study, we noted the vulnerable plaques and re-evaluated in this respect. We have added our results to the text.
5- The protocols and techniques of CT data acquisition (kVp, mAs, Collimation, ...) have to be mentioned, in detail.

The parameters we used during the CCTA screening were added to the text.

6- The City and Country of the CT machine factory are recommended to be stated.

Features of the CT device have been added to the text.

7- Please provide the data about the viewing workstation and the viewing software (e.g., Syngo Via version?)

Image data were evaluated with CT Cardiac Function clinical software application on Syngo Via (version VB 20A) Workstation (Siemens Healthineers, Erlangen, 2019, Germany).

8- How many years of experience in coronary CTA interpretation has the radiologist? Please notify.

A six years' radiologist experienced in cardiovascular disease re-evaluated all CT examinations of the patients.

9- The ethics committee approval number is missing in the main text, while has been written in the Abstract.

The medical ethics committee of our university hospital approved the current study (Approval number:2021/3180).

10- Did the authors correlate the findings and results with Syntax Score, as well? Please clarify.

In our study, the Syntax Score of the patients was not calculated. We have added detailed information in the limitation section about the Syntax score.

11- In Table-1, the interpretations of the CAD-RADS 3 and CAD-RADS 4 as Moderate Stenosis and Severe Stenosis, respectively, are missing. Moreover, the CAD-RADS 5 as Total Occlusion is not mentioned.

As you stated, necessary corrections were made and added to the table about CAD-RADS classification.

CAD-RADS-5 lesion was not detected in any of our patients.

Answers to Reviewer 4:

1**.** Prospective studies are more valuable than retrospective studies, but this does not mean that retrospective studies are worthless. Many retrospective studies in the literature have inspired subsequent prospective studies. It has been included in many retrospective studies in the literature on CAD-RADS scores. We think that our study will be a reference for future studies as a pilot study.

2. Our work is small in size. However, a retrospective CAD-RADS study with a similar number of subjects as our study has recently been published in the literature. We have added this in the limitation section. Our study should be supported by prospective and large population studies. We think that our study will contribute to the literature as a pilot study.

2 Revision 1

3 comments · 16 Oct 2021 – 25 Oct 2021

Referee 1 Reviewer

MAJOR REVISION 16 Oct 2021

Unfortunately, the authors' explanations are not appropriate or convincing.
The first drawback was the inappropriate study design and the use of a cross-sectional design, not the use of retrospective or prospective data. The most important methodological point is that the study design should be tailored to its purpose, which was not the case here. As mentioned in the first review, a cohort study was the best option, followed by a case-control study.
The second issue was related to the sample size, which should be calculated based on statistical assumptions and values from previous studies, using a formula appropriate to the type of study and the statistical nature of the main variable under study.

Associate Editor

MAJOR REVISION 25 Oct 2021

Most of the changes made in the submitted 1st revision meet the requirements based on the queries provided by the reviewers, and the replies are mostly acceptable.
Nevertheless, there are still 2 issues to be concerned about:
1- The methodological points are not appropriately applied.
2- Some spelling and grammatical errors have recently emerged in the text added to the newly submitted version 1 and need to be rectified.

Editor-in-Chief

MAJOR REVISION 25 Oct 2021

Dear authors,
Your article needs Major Revision.
Regards

3

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.

Dear Reviewer,

Thank you for your effort.

1. This study was designed retrospectively and was created as a result of the evaluation of tomography images of 210 patients who applied to our radiology unit between January 2019 and January 2021. The article was not designed as a cohort study or a case-control study because the data were evaluated retrospectively. Between these dates, the data of all patients registered in our center were examined without prejudice. The data were collected with great care.

2. The study is retrospective. After the reviewer's criticism, we again sought the knowledge of two expert statisticians. The experts told us that the study power cannot be calculated in a retrospective study and our sample size was sufficient. We did not know how many patients we would collect between these dates; the number of patients could be less or more. We have meticulously examined all the data between specific dates.

3 Revision 2

2 comments · 5 Nov 2021 – 3 Jan 2022

Associate Editor

ACCEPT 5 Nov 2021

The submitted 2nd revision appropriately responded to reviewers' queries and might be accepted for publication.

Editor-in-Chief

MINOR REVISION 3 Jan 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.

Dear Editor,

Thank you for your letter and for the reviewer and associated editors. We are very happy that we have reached this stage. We have studied these comments carefully and have made corrections that we hope will meet with your approval. The revised components are marked in yellow in the manuscript. The main corrections to the manuscript and the responses to the reviewer and associated editors comments are listed below.

Answer to Reviewer.

1. **In the abstract and text , please insert part of objectives**

   The objective part added to the abstract and main text.

2. ***2.*** **Please cited table 2 in the text.**

   Citation for table 2 has been added to the main text. And the sentence edited as below.

   Sociodemographic characteristics and left ventricular measurement values of the patients are given in table 2.

Answer to Associate Editor 1.

The submitted 2nd revision appropriately responded to reviewers' queries and might be accepted for publication.

Thank you for your evaluation.

Answers to Associate Editor 2.

1-please add full term of abbreviations in the title.

The full term of abbreviations added to the main text. And the sentence edited as below.

Monocyte to High Density Lipoprotein Ratio may Relate to Coronary Artery Disease-Reporting and Data System Score and Increased Left Ventricular Mass.

3-please add objective part to the abstract.

The objective part added to the abstract and main text.

5-please replace the word "introduction" with "background". In addition, please add objective part to the paper.

The background word added to the main text instead of introduction word.

6-what is the meaning of dimension? do you mean diameter ?

The word ‘’dimension’’ has been replaced with ‘’diameter’ in the main text as you mentioned.

7-what is the meaning of "Standard values"?

This words (standard values) has been removed from the text because there is a number representing the standard value (0,6) in the formula.

8-please correct: “All statistical tests” to: “All statistical analyses”

Word correction done in main text

9-please add full terms of abbreviations for the first time [for example ANOVA]

Added full terms of abbreviations to the main text where they were first used.

10-please add manufacturer data of SPSS.
The manufacturer of SPSS program added to the main text like below.

All statistical analyses were performed using the SPSS version 20 program (IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp).

11-this sentence is unclear: “MHR for predicting CAD-RADS score has been evaluated by the receiver operating characteristic (ROC) curve.” May be, it could be improved as: “diagnostic efficacy of MHR for predicting CAD-RADS score has been evaluated by the receiver operating characteristic (ROC) curve.”

It has been added to the main text by making the correction you have specified.

12-authors mentioned: “The number of men in CAD-RADS-2,” it seems better to replace number with frequency. This pattern seems to be applicable in other similar instances such as: “The number of patients with diabetes” or “The number of patients with hypertension”

It has been added to the main text by making the correction you have specified.

13-this part does not have verb: “LVMI of CAD-RADS-2 higher than CAD-RADS-0”

The sentence with grammatical errors was rearranged.

14-please correct: “AUC=0.753, 95% confidence interval [Cl]=0.628–0.878”

The edits you specified were made and added to the main text.

15-please correct: “AUC=0.879, 95% Cl=0.813–0.946”

The edits you specified were made and added to the main text.

16-please correct: “AUC=0.811, 95% Cl=0.717–0.905”

The edits you specified were made and added to the main text.

17-please correct: “AUC=0.739, 95% Cl=0.652–0.826,”

The edits you specified were made and added to the main text.

18-please add space in this part: “showsantioxidant”

It was added by making the necessary word arrangement in the main text.

19-please delete these titles: Limitation study and 5. Conclusion

These titles have been removed from the text

20-what is the meaning of this part: “The results may have been affected”

As you stated, this sentence was removed from the text because it was not suitable for the general text.

21-please correct analyzes to analyses.

Word edited and added to main text.

23-the word “Coroner” in table 2 legend is wrong

The word "coronary" was edited and added to the main text.

24-please correct Anova in footnote of table 2 and 3 to ANOVA

The word (Anova) in the tables is arranged in capital letters.

25-what is109/µL in table 3?

Necessary corrections (10^9) were made and added to the main text.

26¬-please add explanation for ** in table 3.

Necessary corrections (0.48 (0.28-0.70)*) were made and added to the main text.

27-please correct table 4 legend as: "Correlation Coefficients of MHR and LVM with important variables" [or something like this].

As you stated, table 4 legend changed and new legend added to the main text.

**28-please correct table 5 legend: Regression analysis for prediction of …….
[please add the dependent variable in …….]**

As you stated, table 6 legend changed and new legend added to the main text.

29-this legend seems wrong: "ROC curve analysis suggested that the optimum MHR level cut-off point for CAD-RADS-3." The other ROC curve legends are wrong too. Please correct them.

As you stated, figure legends rearranged.

Figure 3.

A,Receiver operating characteristic (ROC) curve of MHR for predicting CAD-RADS-1;

B, ROC curve of MHR for predicting CAD-RADS-2;

C, ROC curve of MHR for predicting CAD-RADS-3;

D, ROC curve of MHR for predicting CAD-RADS-4;

AUC, Area under curve

30-what is the number of patients? 210 or 160? Both have been mentioned.

Although a total of 210 patients were included in the study, 50 patients were excluded

from the study in accordance with the exclusion criteria, so 160 patients were included in the study.

31-Please cited table 2 in the text.

Citation for table 2 has been added to the main text

4 Revision 3

1 comment · 10 Jan 2022

Editor-in-Chief

ACCEPT 10 Jan 2022

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