Author’s response to reviews

Title: Prevalence and associated factors of subclinical atherosclerosis in rheumatoid arthritis at the university hospital of Kinshasa.

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Detailed answers to the reviewers of manuscript BRHM-D-17-00039

Prevalence and associated factors of subclinical atherosclerosis in rheumatoid arthritis at the university hospital of Kinshasa.

Editor Comments:

The two reviewers raised several points. Some of them have already been discussed in previous revisions of the paper. Some are more essential than others of course. By having two new independent reviewers I would like to provide you the option of a fresh view.

In any case, it is of high importance, as mentioned by reviewer 4 to let your article proof-read by an English native speaker.
Please submit a manuscript version that was edited using the track changes mode, as well as a point by point response. This is essential for any further processing of this submission.

A/ we thank the editor for his comments. The article was read by two native English speakers and the different misspellings have been corrected.

Reviewer reports:

Ivan Padjen (Reviewer 3): General comment: The manuscript contains minor orthographic omissions and language errors that require correction.

A/ we thank the reviewer for this general comment. The minor orthographic omissions and language errors have been corrected

Specific comments:

Comment 1 (Abstract, Background, line 2): Perhaps it would be more appropriate to replace the term "early atherosclerosis" with "premature atherosclerosis".

A/ we have replaced the term early atherosclerosis by premature atherosclerosis

Comment 2 (Abstract, Results): Please specify the meaning of "a" in the abbreviation "ORa". If it pertains to "adjusted", it should be indicated when mentioned for the first time in the abstract. Furthermore, since the abbreviation "aOR" is used later in the text in the same context (also in Table 4), it would be useful to consistently use the same abbreviation in both cases (both in the abstract and in the text and Table 4).

A/aOR means adjusted odds ratio. We have corrected in the abstract and the table 4.

Comment 3 (Keywords): UHK is not a standard abbreviation, so it should be explained. Furthermore, it is not common to include an institution's name as a keyword, so perhaps it would be more appropriate (and useful for the readers) to replace this keyword with another term related to the content of the paper.

A/ we have replaced UHK (as a keyword) by cIMT
Comment 4 (Background, third paragraph): Why is it important to analyze the relationship between atherosclerosis and RA in the Democratic Republic of Congo? This association has already been established elsewhere. If the authors still believe (and want to convince their audience) that this matter still requires attention, perhaps it would be useful and interesting to comment on the magnitude of the problem of atherosclerosis (including its complications and related mortality) in the overall population of the Democratic Republic of Congo. Are there any differences between the metabolic syndrome in Congo compared to other parts of Africa and the world? Since causes of death and the profile of mortality/morbidity is probably different in Congo compared to some other parts of the world, addressing these issues would increase the value of this paper.

A/ It doesn’t exist a previous study on the atherosclerosis in the general Congolese population. The present clinical study is the first which has assessed the atherosclerosis Congolese RA patients. Previous studies have shown that RA is less severe in Congolese than in Caucasians for example. So, the fact that the association between RA and atherosclerosis has been established elsewhere is not a reason for not performing the present study. We precise also that a case control study is in progress to assess the metabolic syndrome in rheumatoid arthritis.

Comment 5 (Methods): Please indicate the exact healthcare facility where RA patients were recruited (i.e. Rheumatology department, outpatient clinic etc.).

A/ the RA patients were recruited in the University Hospital of Kinshasa.

Comment 6 (Methods): Joint erosions on X-ray were considered as one of the prerequisites to classify a patient as having severe RA. Since only hand X-rays were specifically mentioned in the last paragraph of the Methods section (before the section "Definition of some concepts"), please indicate if erosions at other sites (e.g. feet) have also been taken into account.

A/ only data on hand x-rays were available.

Comment 7 (Methods): Since both ESR and CRP were measured, please explain why both DAS28-ESR and DAS28-CRP were not calculated and included in the analysis.

A/ We confirm that the DAS-28 ESR was calculated and included in the analysis. See tables 1 and 3.

Comment 8 (Methods): The unit "mega Hertz" can be replaced with its standard abbreviation.
A/ Mega Hertz unit has been replaced by its standard abbreviation MHz

Comment 9 (Results, Table 3, legend, row 3): the word "erythrocyte" after the "erythrocyte sedimentation rate" is redundant.

A/ the word erythrocyte after sedimentation rate has been deleted

Comment 10 (Results, Table 4): If "aOR" is an abbreviation of "adjusted odds ratio", this should be clearly indicated in the table legend. Furthermore, according to which variables was the OR adjusted?

A/ the meaning of aOR has been clearly indicated in the legend of table 4

Comment 11 (Discussion, page 6, last sentence of paragraph 1): Perhaps it would be more precise to state that chronic inflammation is the basis of long-term progression of RA.

A/ in page 6, paragraph 1, the last sentence has been modified like this: “So, chronic inflammation is the basis of long-term progression of RA which is closely linked to the development of subclinical atherosclerosis”.

Comment 12 (Discussion, page 6, paragraph 4): Please replace the term "ultransensible" with "ultrasensitive" (CRP).

A/ the term ultrasensible has been replaced by ultrasensitive

Comment 13 (Discussion, Limitations): The authors should also address the issue of whether their sample is representative of the Congolese population of RA patients. Are there concerns that RA may be underrecognized/underdiagnosed in the Democratic Republic of Congo, especially given the issue of social differences and consequent inequity in access to healthcare/rheumatology care? Furthermore, the authors should clarify if their institution is a tertiary level healthcare facility and whether there is an existing rheumatology service at a secondary level.

A/our sample is not representative of the Congolese population with RA. We said it in the limits of this study. The disease is underdiagnosed because of a limitation of access to care. This study was carried out in the university hospital of Kinshasa who is tertiary level with a rheumatology
service. At the secondary level we have also rheumatology services run by rheumatologists. For the time being the country has a total of seven rheumatologists.

Summary opinion:

The manuscript has been submitted to BMC Rheumatology as a research article. The authors have assessed the frequency and associated factors of subclinical atherosclerosis in RA at a university hospital in the Democratic Republic of Congo (DRC).

The most important value of this paper is not the fact that it assesses subclinical atherosclerosis in a group of RA patients (although the topic is clinically relevant per se), but the setting of an emerging country where the study has been carried out. For this reason, it would be valuable to emphasize some more "local" issues, such as the magnitude of the problem of atherosclerosis in the DRC.

The manuscript has been clearly written and the analysis of data has been presented in a simple and clear manner.

A/ we thanks the reviewer for this summary opinion

Helga Radner (Reviewer 4):

Although the topic of the study is of great importance the study itself has many limitations: it would require a native speaker to fix typos, errors of grammar and style etc

A/ / we thank the reviewer for his comments. The minor orthographic omissions and language errors have been corrected.

1. Would mention studies already assessing risk of atherosclerosis in RA patients. What is the novelty of this study beside the fact that it is studied in the DRC?

A/ The importance of this study is the fact that this is the first study in our country that allowed evaluating atherosclerosis in RA patients. This study allowed us to make a state of place for future studies.

2. p2 second paragraph: "This high frequency of CV morbidity.. «Not well formulated. Do you talk about incidence, prevalence or the higher risk?"
we are talking about a high incidence. We have corrected this in the text

3. P2 second paragraph last sentence ’ … are also major cardiovascular risk.’ ??factors? Drivers of risk??
A/ we have deleted “are” from this sentence. :

4. I would strongly recommend to change to outline and formatting of this section; the section 'definition of some concepts' is very unusual and does not make much sense to me.
A/ we thank the reviewer for this suggestion, although the definition of the concepts, is unusual it seems important to us in understanding of this study.

5. Alcoholism is not a CV risk factor
A/ according to the literature ,it appear that moderate consumption of alcohol seems to be associated with a lower risk of coronary disease, while higher consumptions seem to increase this risk.

6. Severity defined by HAQ>0.5 - what is the rationale behind that? Seems like an arbitrary cut-off to me..
A/ We defined the severity of the disease by a HAQ value of ≥ 0.5 in reference to recommendations for other African populations: see recommendations of good medical practice, Moroccan Society of Rheumatology, ALD number 26,September 2011;page 19 and line 13.work group : Pr. Abdellah El Maghraoui et al.

7. Statistical analyses needs to be better explained
A/ we believe in our humble opinion that statistical analyses are better explained.

8. - Sample size too low to perform regression analyses including > 8 different covariates. Are covarites included independent - problem of colinearity?!
A/ we admit that the small sample size reduces the power of statistical tests. The included variables were independent. After collinearity testing, the metabolic syndrome, diabetes and hypertension were all collinear. This means that the metabolic syndrome has not been included in the model.

9. Again, results are not presented very well; re-writing required

A/ we think the reviewer for this suggestion; we have tried to correct the presentation of our results as far as possible.