Author's response to reviews

Title: Profile and course of early Rheumatoid Arthritis in Morocco. A two-year follow-up study.

Authors:

benbouazza Karima (kbenbouazza@yahoo.fr)
benchekroun bahia (benchek_1@yahoo.fr)
rkain hanan (hanankain@yahoo.fr)
amine bouchra (amine_bouchra@yahoo.fr)
bzami fatiha (bzamifatiha@yahoo.fr)
benbrahim leila (l.benbrahim@yahoo.fr)
atouf ouafa (atoufoufa@gmail.com)
essakalli malika (m_essakalli@hotmail.com)
abouqal redouane (abouqal@invivo.edu)
dougados maxime (m.doug@cch.aphp.fr)
hajjaj-hassouni najia (nhajjajhassouni@gmail.com)

Version: 3 Date: 26 September 2011

Author's response to reviews:

Replies to the Reviewer:

Replies to the reviewer 1:

We would like to thank you for your analysis of this work and your comments which help us to improve the quality of the manuscript.

Below are the answers to each specific point.

The major concern of this study analyzing the clinical and radiological evolution of an RA cohort in Morocco is the small sample size. The number of patients (n=51) is very low to obtain valid data about prognostic factors of structural damage in this population, that is one of the major aims of the study.

We agree with you concerning data about predictor factors of structural damage. To put the emphasis on the difficulties to analyze predictor factors in such small cohort, it is now written. P: 12; L: 11-12.

This observed lack of association between radiographic progression and different factors shown in literature could be due to a lack of power.

We are well aware that this is a study of a small number of patients with early rheumatoid arthritis (RA). There have been many larger studies of RA. Where it is unique is in its geographical setting - namely in North Africa. Thus, this study give to our opinion a global description of an unusual cohort of early RA patients.
treated in an area where medical care is difficult to provide.

Another major concern is if this RA cohort is representative of the RA population in this country. The author should clarify this point.

Patients included in the study were either hospitalized or seen in the outpatient clinic in El Ayachi hospital. This public healthcare structure is the first referral hospital of Rheumatology in Morocco. Patients included were originary from different regions of our country. Thus, this RA cohort is surely representative of the RA population in our country.

We added the following passage in the materiel and patients section. P: 4; L: 18-22.

Patients were followed by their rheumatologist and addressed for assessment as outpatients in El Ayachi hospital (public structure and referral hospital of Rheumatology in Morocco where hospitalizations and outpatient clinics are accessible for patients originary from different regions of our country) at baseline and 2 years thereafter.

Minor:

- Demographic data of this population raised several questions or comments:

  1. mean age is 46 and, as the authors comments in the discussion, this is significantly lower than those observed in other countries. This is the same in other arabian populations?

  Unfortunately, there is a complete lack of data of early RA Arabian cohorts. This is why it wasn’t possible to do such comparisons.

  2. The disease duration is "only" 24 weeks. This seems to me low according to the socioeconomic status of this population.

  24 weeks doesn’t correspond to the disease duration. It’s the mean delay of referral to specialist.

  3. the difference between tender and swollen joint counts is higher than expected. Why?.

  Clinical exam was performed by experimental rheumatologists. The high difference between tender and swollen joint counts could be explained by a small size of synovitis or by the lack of precision from patients who overestimate their pain.

  4. HAQ is very high at baseline, suggesting a very disabling disease, but decrease dramatically after two years. How do the authors explain this dramatic improvement?
We think that significant improvement of functional disability at 2 years can be explained by the good evolution of patients under DMARDs.

- The rates of remission is similar to those observed in other studies of early RA after DMARDs. However there is no data of disease activity through the follow-up, making the interpretation of these data very difficult.

Because of technical and financial considerations, we have not included in the design study regular assessment throughout the 2 years of follow-up. Thus, we were not able to precise informations related to disease activity through the follow-up. We have noted this precision in the original manuscript.

- Patient were trated mainly with MTX. Can you provide the mean doses of this drug?

Yes, of course. Patients received IM injections of MTX at a dose of 15mg once a week. We added the following precision in the revised manuscript. P: 8; L: 2.

Methotrexate (MTX) was the most frequently prescribed DMARD, being taken at a dose of 15 mg once a week by 65.2 % of patients and followed by Sulfasalazine and Chloroquine (10.8 % for each of them).

- The classification of radiographic progressors and progresors seems to me adequate, but the interpretation of the data on prognostic factors, as the authors comment in the discussion is very difficult, almost impossible taking into account the sample size.

That is correct. To put the emphasis on the difficulties to analyze predictor factors in such small cohort, it is now written. P: 12; L: 11-12.

This observed lack of association between radiographic progression and different factors shown in literature could be due to a lack of power.

A larger multicentric cohort, which is ongoing actually, will permit to us in the future a better analysis and a global view of prognosis factors.

- The discussion is long and merits to be shortened. Also the discussion should be addressed about the differences of the clinical evolution of this population in comparison with other RA populations of similar ethnic origin.

As recommended, we have as far as possible deleted some passages from discussion to let it shorter.

At our knowledge, there are no other RA cohorts published in other countries of similar ethnic origin. By consequent, there is no possibility to apply the second recommendation.

Replies to the reviewer 1:
We would like to thank you for your encouraging analysis of this work. Our answers and commentaries are as following:

MINOR IMPORTANT COMMENTS

1. Abstract numbers
Are results range or inter quartile range?
Some results were expressed by means. Others were expressed by medians.

2. Abstract
How can mg of prednisone for patients taking prednisone be 0-8? It should be 1-8…Please check.

Yes, this was corrected.

3. Abstract prediction: is JC swollen or tender?
We are sorry for this omission. Swollen has been added in the revised manuscript.

4. Methods: is follow up at 1 and 2 years (see lost to follow up) or only at 2 years? Please clarify.
Thank you for your precision. Sentence was reformulated.

Fifty one patients (45 women, 6 men) were enrolled in this study. Six patients (1 patient died, 5 refused further follow-up) were lost to follow-up at 2 years. Data on 45 patients were thus available for analysis 2 years after their inclusion in the study. P:7. L: 6-8.

5. Radiographic scoring – please state which score was used.
Structural damage was assessed by counting the number of erosions and grading the joint space narrowing (JSN) according to the Sharp and van der Heijde method.

We add this precision in the modified manuscript. P: 6; L: 3.

6. Results: how can parity in women with children be 0 to 5? Is this range or interquartile range? In both cases it should be 1-5 please check. It's interquartile range;

We agree with you that data concerning parity did not bring new knowledge. Thus, we have removed it.

7. Table 1 would be more informative by showing all patients / progressors / non-progressors.
Since table 1 shows patients characteristics at inclusion, we think that’s too early to introduce at this step progressor and non progressor patients.

8. Discussion: for me the main results are not prediction (since because of small sample size nothing is significant – this should indeed be clearly discussed) but rather remission prevalence and lack of erosions in this cohort. Please discuss these points.

That is correct. To put the emphasis on the difficulties to analyze predictor factors in such small cohort, it is now written. P: 12; L: 11-12.

This observed lack of association between radiographic progression and different factors shown in literature could be due to a lack of power.

We have made the revised manuscript clearer regarding remission prevalence and lack of erosions in this cohort.

Just for precision, another manuscript focused on remission under DMARDs in this cohort has been recently published in joint bone spine journal.

10. Discussion: please discuss if hospital is free for all and how patients have access to treatment in Morocco. Could this have induced bias?

Since health care services are not affordable for a large part of the Moroccan population. Almost of biological and radiographical charges were supported by the Hassan II Academy of Sciences and the Ibn Sina Universitary hospital.

11. Discussion: the paragraph about children could probably be deleted (it does not bring new knowledge).

As recommended, we have deleted the paragraph about children in the discussion.

12. The discussion is too long and should be otherwise shortened by a page or so.

As recommended, we have deleted, as far as possible, some passages from discussion to let it shorter.

MINOR COMMENTS

Please define abbreviations in the abstract (RA, STVDH).

We would thank you for this precision. We define abbreviations in the abstract (RA: rheumatoid arthritis, SVDH: Sharp and van der Heijde.

Please add Das remission in abstract instead of remission.

As recommended, we add Das remission in abstract instead of remission.
Please check the English eg high scarcity (intro), parity (wrong term) in Methods, ACPA instead of anti CCP (methods), evolution (please say progression) in Results.

We are sorry for those English faults. We replace the words cited as following:

- High scarcity (intro) by There is a lack of research.
- Anti CCP in methods was replaced by ACPA.
- Evolution in Results was replaced by progression.

3. 1987 RA criteria in methods since there are new ones.

We are well aware that this the new criteria should be used instead of the ACR 87 criteria. However, those criteria were difficult to apply in time of patients' recruitment.