Author's response to reviews

Title: Long-term renal outcome in patients with malignant hypertension: a retrospective cohort study

Authors:

   Fouad Amraoui (f.amraoui@amc.nl)
   Sarah Bos (bos.sarah@gmail.com)
   Liffert Vogt (l.vogt@amc.nl)
   Bert-Jan H. van den Born (b.j.vandenborn@amc.nl)

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Author's response to reviews: see over
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Title: Long-term renal outcome in patients with malignant hypertension: a retrospective cohort study

Dear Editor,

First of all we would like to thank the editorial board for the opportunity to revise our manuscript. We thank the reviewers for their positive and useful comments which helped in further improving our paper. We addressed all remarks and disclosed an itemised list below.

We hope that the current version of our manuscript can be considered for publication and look forward to your decision.

Thank you in advance for your time and consideration.

With kind regards, on behalf of all authors,
Fouad Amraoui
Reviewer 1:
Comment 1
‘The proportion of patients developing ESRD was not significantly different between those having primary malignant hypertension and those with primary renal or renovascular disease (24% vs. 38% respectively, P = 0.18).’ The study power does not seem to be sufficiently powered for such comparison and the trend is (as perhaps expected) towards the higher rates in those with secondary MHT.

We agree with the reviewer that although ESRD was not significantly more common in patients with primary renal or renovascular disease, there was a trend towards a higher incidence of ESRD in these patients. We therefore added a phrase in the limitations section stating that our study may be underpowered to draw a definitive conclusion on this matter.

Comment 2
Follow-up BP was adequately controlled in only 31% of participants, a rather low value. It could be related to suboptimal compliance, particularly among the ethnic minorities, which were not minorities in this study. Obviously, it would be probable impossible to assess the compliance retrospectively, but this should be discussed more thoroughly.

Although addressed in a previous publication, we agree with the reviewer that the issue of compliance should be discussed more extensively. We therefore added a section in the discussion and included references.

Comment 3
Please specify which echocardiographic criteria of left ventricular hypertrophy were used.

For this study left ventricular hypertrophy was considered present when diagnosed by a cardiologist. In our hospital, left ventricular wall thickness is measured with a cut-off value of 11 millimeters. We have added this information to the methods section of our paper.

Reviewer 2:
Comment 1
The impact of racial and social differences on clinical presentation and outcome is somewhat stated but not satisfactorily clarified.

In our previous publication entitled: ‘Ethnic disparities in the incidence, presentation and complications of malignant hypertension,’ we focused on the impact of racial and social differences on the clinical presentation of patients with malignant hypertension. We agree with the reviewer that although ethnicity was accounted for in our Cox regression analysis, this issue could have been discussed more thoroughly. Therefore we added a section in the discussion and provided additional data on the ethnicity of patients who reached the primary endpoint within 3 months after admission and who were thus excluded from Cox regression analysis. We also provided additional data on ethnic differences in blood pressure control during follow-up.

Comment 2
Similarly, adherence to therapy and type of medications seem to be a significant component of the outcome and this should be discussed in more detail.
In particular the data of table 2 show a reported mean BP of 146-90 mmHg, but with 50% of patients off target, less than 70% of patients on active treatment and apparently no patient on combined or triple therapy. These data are of interest but should be discussed more extensively.

We agree with the reviewer that a detailed description of the antihypertensive treatment of our patients is very relevant for this paper. We noticed by reviewing our data that the variables concerning antihypertensive drugs in table 2 (except the number of patients on ACE/ARB) were actually baseline data. We adjusted table 2 by replacing the baseline data by the follow-up data. In addition a more detailed description of the mean blood pressure during follow-up was provided in this table by adding the number and percentage of patients in each hypertension category.

Finally, data in table 2 are further clarified by mentioning the total number of patients that was used to calculate the percentages as data on follow-up BP and antihypertensive treatment could only be retrieved for 92 (87%) of patients.

Reviewer 3:

Comment 1
Are there some differences in the requirements of antihypertensive drugs between patients with controlled and uncontrolled BP during the follow-up?

In response to this interesting question we analysed the mean number of antihypertensive drugs among those with controlled and uncontrolled blood pressure during follow-up. These data are added in the results section of our paper.

Comment 2
Are there some data about changes in albuminuria-proteinuria during the follow-up?

We agree with the reviewer that this information would improve our paper. Unfortunately, data on follow-up proteinuria could not be analysed because urine analysis was performed on different time points, with different testing methods making it very difficult to analyse retrospectively.

Comment 3
Considering that blockade of renin-angiotensin system is associated with favourable renal outcome in malignant hypertension, are there some explanations for the low percentage (54%) of patients receiving ACE inhibitors or ARBs?

We agree with the reviewer that 54% would be a low percentage. By reviewing our data we noticed that we mistakenly used baseline anti-hypertensive drug use instead of the follow-up data on BP lowering drugs. The actual % of patients on ACE/ARB was 80%. This figure is depicted in table 2 along with the other drug classes used during follow-up. We apologize for the confusion.