Author's response to reviews

Title: Renal dysfunction, restrictive left ventricular filling pattern and mortality risk in patients admitted with heart failure: A 7-year follow-up study

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Author's response to reviews: see over
Itemized response letter

Reviewer’s report

Title: Renal dysfunction, restrictive left ventricular filling pattern and mortality risk in patients admitted with heart failure: A 7-year follow-up study

Version: 4 Date: 2 August 2013

Reviewer: Alberto Palazzuoli

Reviewer’s report:
The revised article by Schou et al. has now improved in most of parts, and methods limitation are now extensively reported following reviewers suggestions. I much appreciated the insertion of Multivariate cox model adjusted for clinical risk factor. Although the paper is original and interesting as I previously written, two major points remain to be clarified.

1. authors don not distinguish patients with impaired and preserved systolic Function

Our response:

We have in the multivariate models adjusted for LVEF and have also tested for an statistical interaction between LVEF, RF and mortality risk, so we think we have taken account for LVEF in our analyses and in the manuscript. We did not divide the patients into subgroups of LVEF since we did not find any statistical interaction between LVEF, RF and mortality risk

We agree with Reviewer 1 that it can be stated more clearly in the manuscript and have therefore changed the revised version at page 8

From:

“Furthermore, we did not observe any interaction between mortality risk, RF and ischemic versus non-ischemic cardiomyopathy (P>0.05), between mortality risk, RF and history of hypertension (P>0.05) and between mortality risk, RF and LVEF > 40 % (P>0.05).”

To:

“Furthermore, we did not observe any interaction between mortality risk, RF and ischemic versus non-ischemic cardiomyopathy (P>0.05), between mortality risk, RF and history of hypertension (P>0.05) and between mortality risk, RF and LVEF > 40 % (P>0.05). The prognostic significance of RF did, therefore, not interact with any of these important subgroups for which reason the patients were not divided further into subgroups”
2-definition of restrictive filling pattern based only on DT is incomplete

Our response:

We agree with Reviewer 1 that it is incomplete and have already written about the issue in the limitation paragraph.

Based on the comment from Reviewer 1 we have changed the limitation paragraph at page 12

From:

“Furthermore, we defined severe diastolic dysfunction solely by RF and do not have data on left ventricular hypertrophy or tissue Doppler variables and it may therefore be argued that our results reflect inaccurate measurement of GFR and misclassification of severe diastolic dysfunction. However, recently it has been questioned whether a gold standard for diastolic function exists at all(40) and RF may be a reasonable estimate due to its extensive documented association with mortality risk in patients with HF and myocardial infarction(35,36).”

To:

“Furthermore, we defined severe diastolic dysfunction solely by RF and do not have data on left atria volume, left ventricular hypertrophy or tissue Doppler variables and it may therefore be argued that our results reflect inaccurate measurement of GFR and misclassification of severe diastolic dysfunction. However, recently it has been questioned whether a gold standard for diastolic function exists at all(40) and RF may be a reasonable estimate due to its extensive documented association with mortality risk in patients with HF and myocardial infarction(35,36). Though, misclassification of severe diastolic dysfunction may have occurred due to lack of data on left atria volume, left ventricular hypertrophy and tissue Doppler”

We have also changed the conclusions at page 12

From:

“In HF patients severe diastolic dysfunction does not explain the increased mortality risk observed with decreasing eGFR. Factors other than impaired left ventricular filling explain the association between renal dysfunction and mortality risk. Whether the effect of eGFR and mortality risk in HF per se is causal deserves further study as does the potential impact of renal sparing strategies in this group of patients.”

To:

“In HF patients restrictive filling of the left ventricle does not explain the increased mortality risk observed with decreasing eGFR. Factors other than impaired left ventricular filling explain the association between renal dysfunction and mortality risk. Whether the effect of eGFR and mortality risk in HF per se is causal deserves further study as does the association between eGFR and diastolic function in HF.”
Minor points some grammar mistakes in the reference need to be corrected

Our response:

It is corrected.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Our response:

We have run through the manuscript and improved the language and corrected spelling and typographical errors

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Reviewer's report

Title: Renal dysfunction, restrictive left ventricular filling pattern and mortality risk in patients admitted with heart failure: A 7-year follow-up study

Version: 4 Date: 20 July 2013

Reviewer: Gillian Whalley

Reviewer's report:
The authors have addressed all of my concerns.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare i have no competing interests
Dear Editor at BMC Nephrology,

Enclosed is a second revised version of the manuscript:

Renal dysfunction, restrictive left ventricular filling pattern and mortality risk in patients admitted with heart failure: A 7-year follow-up study

We have implemented the comments from the reviewers and think the manuscript has been much improved and think it is suitable for publication BMC Nephrology.

Enclosed is also an itemized response letter.

We allow us to re-submit it to your journal since we find the issue it deals with relevant for the readers of your journal. We think our data provide new insight into the association between renal function and mortality risk in heart failure. Renal function is not a surrogate for diastolic dysfunction and diastolic dysfunction does not affect the prognostic significance of renal dysfunction. More research in renal sparing strategies is, therefore, needed based on our results.

Author contributions:

Morten Schou: hypothesis, data analysis and manuscript preparation; Jesper Kjærgaard: data collection, data analysis and manuscript preparation; Christian Torp-Pedersen: data collection, data analysis and manuscript preparation; Christian Hassager: data collection, data analysis and manuscript preparation; Finn Gustafsson: hypothesis, data analysis and manuscript preparation; Dilek Akkan: data collection, data analysis and manuscript preparation; Jacob E Moller: data collection, data analysis and manuscript preparation; Lars Køber: hypothesis, data collection, data analysis and manuscript preparation.
All authors have approved the final manuscript and submission to BMC Nephrology.

We are looking forward to hear from you

Sincerely yours,

Morten Schou, MD, PhD

Corresponding Author