Author’s response to reviews

Title: Morning blood pressure surge and target organ damage in newly diagnosed type 2 diabetic patients: A cross sectional study

Authors:

Johanne Lyhne (JohanneLyhne@gmail.com)
Esben Laugesen (esben.laugesen@clin.au.dk)
Pernille Høyem (pernillehoeyem@hotmail.com)
Simon Cichosz (simon.cichosz@clin.au.dk)
Jens Christiansen (jsc@clin.au.dk)
Søren Knudsen (stk@dadlnet.dk)
Klavs Hansen (klavhans@rm.dk)
Troels Hansen (troels.krarup.hansen@clin.au.dk)
Per Poulsen (d243205@dadlnet.dk)

Version: 1 Date: 22 Oct 2015

Author’s response to reviews:

Dear Executive Editor Tim Shipley and reviewers

Thank you for your positive evaluation of our manuscript and for the many constructive comments provided. We have now thoroughly revised the manuscript according to the comments and implemented the suggested changes, and we believe this to be a considerably improvement of our work – thank you again.
Reviewer #1:

Thank you for the highly relevant comments, which we have addressed as follows:

1) As suggested by the reviewer, we have stated that “Furthermore, the diabetic patients had a relatively low PWV and UAE, and the range was quite narrow for both. Thus the chance of finding a signal is reduced” in a small section after the discussion.

2) We have described the rationale for the adjustments in the statistical section as suggested by the reviewer. “In all multivariate analyses, we adjusted for age and sex, and in analyses in the pooled sample additionally for the effect of diabetes (yes/no). Blood pressure levels may confound the association between morning surge/systolic night-day ratio and the three outcomes (PWV, UAE and WML). Accordingly, the effect of including 24-h systolic BP in the analyses with age and sex was also evaluated in supplementary analyses. PWV is also known to be associated with office mean BP and heart rate, and the effect of including these parameters together with age and sex in the analyses with PWV as outcome was also assessed.” Additionally, in the results section, we have clarified that all analyses were adjusted for age, gender, 24-h SBP and diabetes, and PWV analyses were further adjusted for mean arterial pressure and heart rate at time of measuring.

Reviewer #2:

Thank you for your comments on our study design and our power calculations. The comments are highly relevant, and we have tried our best to address these major points:

1) This study is a cross sectional study. We have included the description “a cross sectional study” in the title, as suggested in the instructions for authors. Newly diagnosed diabetic patients were matched with non-diabetics on age and sex to investigate cerebro- and cardiovascular risk factors. Previous studies on the same sample group have reported a significant correlation between pulse wave velocity and white matter lesions in diabetic patients. In this study we investigate these risk factors further, as we include the morning blood pressure surge and the systolic night-day ratio.

2) Concerning sample size we have described our power calculations in the statistical section. “Not all morning BP surge parameters could be calculated for all participants due to missing BP data during the night. Accordingly, we did power calculations for different potential sample sizes. With 80 participants in each group, a standard deviation of 10 mmHg and a 5 % \( \alpha \)-level, we had 97 % power to detect a difference of 6 mmHg in morning surge between the groups. With 60 participants in each group, a standard deviation of 10 mmHg and a 5 % \( \alpha \)-level, we had 90 % power to detect a difference of 6 mmHg”. And further on added “The lack of the
statistical difference in the subgroups might be a consequence of low statistical power. Our results may not be applicable in other populations” in a small section after the discussion.

Minors: The comment is highly relevant as the description “cohort” is imprecise. The sentence has been chance to “The study sample has been described in detail previously” as this and the previous study are cross sectional. “Briefly” has now been deleted.

We are looking forward to hearing from you again.

Regards,

Johanne Lyhne, MD