Author's response to reviews

Title: Graz Endocrine Causes Of Hypertension (GECOH) study: A diagnostic accuracy study of aldosterone to active renin ratio in screening for primary aldosteronism

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Author's response to reviews: see over
Dear editors of BMC Endocrine Disorders,

We thank you for the knowledgeable review of our manuscript “Graz Endocrine Causes Of Hypertension (GECOH) study: A diagnostic accuracy study of aldosterone to active renin ratio in screening for primary aldosteronism”.

We are grateful for the constructive suggestions given, which helped to improve our manuscript.

We hope that our paper is now suitable for publication in BMC Endocrine Disorders.

Yours sincerely,

Stefan Pilz and Andreas Tomaschitz

See below the changes (marked red in the manuscript), that we have introduced in the manuscript according to the comments of the reviewer.

Reviewer 1:

This is a very thorough and detailed study proposal. I offer several suggestions:

a) Perhaps too much emphasis is placed on the saline suppression test. Can the authors put this test into context for subjects who already have a dietary salt intake with > 200 mEq Na already in the 24 hr urine.

Response: We thank the reviewer for this valuable comment concerning dietary salt intake. Accordingly, we now mention in the manuscript that dietary salt loading has a significant impact on the renin angiotensin aldosterone system with complex interactions and is thus a potential confounder for diagnostic procedures for primary aldosteronism, which are currently largely performed without considering dietary sodium intake. Considering the possible influence of dietary salt loading on the results of the saline infusion test we will perform additional measurements of the 24 hours urine sodium and aldosterone levels in the GECOH study. In patients with 24 hours urine sodium levels above 200 mEq we will evaluate the test characteristics of the saline infusion test in comparison with primary aldosteronism diagnosis based on 24 hours urine aldosterone levels (used cut-off 12µg/24hours for aldosterone urine levels). We believe that this evaluation of the test characteristics of the saline infusion test in the setting of high dietary salt intake will significantly improve the knowledge about the influence of oral salt loading on diagnostic procedures for primary aldosteronism.

b) Primary aldosteronism and resistant hypertension are especially important in
patients of African descent; will these subjects be adequately represented in the GECOH cohort?

**Response:** We agree with this comment of the reviewer and now included in the manuscript that ethnic differences regarding the regulation of sodium balance and the renin angiotensin aldosterone system are of particular interest because previous studies suggest that patients of African ancestry might be predisposed to low renin levels. We therefore do not restrict our study population to certain ethnicities but the low proportion of e.g. persons with African ancestry in Austria may limit our ability to detect ethnic differences.

c) David Calhoun has written extensively about primary aldosteronism and resistant hypertension. His work needs to be cited (Nishizaka, M. K., M. Pratt-Ubunama, M. A. Zaman, S. Cofield and D. A. Calhoun (2005). "Validity of plasma aldosterone-to-renin activity ratio in African American and white subjects with resistant hypertension." Am J Hypertens 18(6): 805-12.).

**Response:** We appreciate the work of David Calhoun about primary aldosteronism and resistant hypertension and included the above mentioned article into our reference list.