Author's response to reviews

Title: Limited value of long-term biochemical follow-up in patients with adrenal incidentalomas - A retrospective cohort study

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Author's response to reviews:

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Dear Ms Cruz,

We thank the two reviewers for their helpful and constructive comments. We have included a detailed response below to the specific points raised. The changes have also been highlighted in the manuscript using track changes.

We think the manuscript has been improved by these changes and we hope you can now consider the manuscript acceptable for publication in BMC endocrinology.

Sincerely yours,

Dr Buster Mannheimer

Reviewer # 1

1. We now state the definition of stationary used:

Lipid poor (over 10 HU on unenhanced series with an absolute washout of more than 50 per cent) small adenomas and large (#3cm) lipid rich adenomas were considered benign if they were stationary (< 20% or ≤5mm increase in diameter) at follow-up of at least 12 months.

2. We now provide information regarding the time window for assessment of absolute washout:

“...with an absolute washout with late series measured 15 minutes after contrast injection of more than 50 per cent”

3. 5. Regarding the exclusion of patients in figure 1 and the number of patients with a complete work up at follow up. This would be an interesting angle. However, the boxes representing different reasons for exclusion are in fact not mutually exclusive but to a rather large degree overlapping. Patients are
excluded in the order that they appear in the flow chart. Lines have been replaced by arrows to clarify this. Thus, the absolute majority of patients with incomplete biochemical testing at baseline did neither have a complete testing at follow up; Although 117 individuals were screened at 24 months follow up, the screening was complete in only 67. Being only slightly larger than the main analysis, and constituting a quite different selection of patients, we believe that the discussed sub analysis is better left out.

4. We have now revised the numbers of patients stated in the last paragraph in the results section so that they match with figure 2.

6. In Table 1, we have now removed baseline data on attenuation and wash-out presented as means and instead provide prevalences on incidentalomas classified as lipid rich, lipid poor with abs >50% and #50% respectively. Thus the table does now better adhere to the classifications in the methods section.

7. The by far most common disorder, at baseline assessment as well as at 24 month follow up was cortisol hyper secretion for reasons of that are thoroughly discussed (methodological problems, variation over time not associated with genuine disturbances etc). However, focusing on 24-months biochemical follow-up in patients with an initial normal screening we feel that in detail data regarding baseline false –positives would be of little additional value and may take the focus from our main message.

Reviewer # 2

1. Being a retrospective evaluation of clinical practice we were unfortunately not able to perform any genetic testing.

2. Yes, we do agree that prospective studies should be performed which is now clarified in the discussion:

“In order to further evaluate the value of long-term biochemical follow-up we do suggest prospective larger studies..”

3. We agree that incidentalomas in younger people are rare and the chance of finding a hormonal disturbance or congenital condition may be increased even though this has not been studied extensively. We have in the revised manuscript added the following sentence in the Discussion section:

“The age of the individuals involved in the current study range from 34 to 94 with few individuals below 50 (n=16) years and the results of the study may therefore not be extrapolated to a younger population. The prevalence of adrenal incidentalomas is rare in individuals < 40 years old, and the chance of finding a hormonal disturbance or congenital condition such as congenital adrenal hyperplasia may be increased [21] but this has to be studied further.”

4. We now define Cushings syndrome and subclinical CS in the methods section:

Cushing’s syndrome was defined as clinical signs typical of Cushing’s syndrome (moon face, buffalo hump, hypertension, osteoporosis, diabetes mellitus) together with two tests of cortisol secretion being abnormal. Subclinical Cushing was defined as two abnormal tests in an individual without clinical signs of Cushing’s syndrome.