Reviewer’s report

Title: C-Peptide and cardiovascular risk factors among young adults in a southern brazilian cohort study

Version: 0 Date: 24 Jan 2018

Reviewer: Margareta Hellgren

Reviewer’s report:

Interesting data but needs a major revision. The paper is a complex and would benefit from a more straightforward approach, like concentrating on type 2 diabetes. That the associations between risk factors and C-peptide is different between type 1 and type 2 diabetes is expected, due to the mechanism, and if you want to mention both types of diabetes you need to add that this difference is expected. In my perspective, the most interesting part is that this is a young population and that already at this age an increased C-peptide is associated with risk factors like C-reactive protein.

In methods it is mentioned that a rapid weight gain between 2 and 4 years is reported and it would be of great interest if a rapid weight gain at this age is related to a high C-peptide at the age of 23 and 30 years. Is this analysed?

Comments

Major:

As we know or at least find it very likely that an increased C-peptide is associated with cardiovascular disease (CVD) it is actually not very interesting to know whether it is associated with risk-actors for CVD. Still, the age of the participants makes it more interesting. That already at this age it is possible to see an association between C-peptide and risk factors, it would be worthwhile to mention this in the discussion.

You mention that this is a population followed since birth, a prospective longitudinal study. Though, data from the early years is not used as predictors, not even the rapid weight gain, between 2 and 4 years, is used as a possible predictive factor. From the age of 23 to the age of 30 it is longitudinal but you don’t report if it is the same population at these two occasions or if the follow-up has addressed even participants who did not participate at the age of 23. It would also be interesting to know if any factors (i.e. CRP), at the age of 23 predict an increased C-peptide at the age of 30.

Minor:

Background
1. You write that 3/4 of the deaths from CVD occur in low, or medium income countries. It would be of value to know how high percentage of the population that live in these countries.

2. You write quite a lot about type 1 diabetes and that is ok but if you want to discuss both type 1 and type 2 diabetes you need to mention that these differences concerning C-peptide is expected.

Methods

1. I would like to know how many (if any) of the participants that had type 1 or type 2 diabetes at 23 and at 30 years of age.

2. Is it the same population that is examined at the age of 23 and the age of 30?

3. If the participants have any serious chronic diseases this should be mentioned

4. Did the participants use any medication?

Results

1. Did not quite understand what you meant with "...given the 325 identified in the cohort..." Where there 325 deaths?

2. Table 1. Don’t give decimals at the length data, now they seem do become taller at 30 years than at 23 years, which is not very likely.

3. Prevalence of a sedentary lifestyle seem to have decreased very much from 23 to 30 years. This is not what we usually see. Have you mixed the numbers possibly? It is possible that it is correct of course, just want to make sure.

4. Concerning table 2 it needs a little more explanation. Is the P-value for trend?

Discussion

As mentioned before the conclusion is actually expected. It would be more interesting with a discussion concerning the development of type 2 diabetes and the age perspective, of if you can find predictive factors for an increased C-peptide at 30 years of age.

Good luck with the revision!

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.
Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Unable to assess

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

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