Reviewer’s report

Title: Adiposity markers and risk of coronary heart disease in patients with type 2 diabetes mellitus

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Reviewer: Nuno n.m.P Pimenta

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Comments to the authors:

Tonding et al. presented a paper entitled “Adiposity markers and risk of coronary heart disease in patients with type 2 diabetes mellitus”. The aim of the study was to evaluate the potential association between body composition markers and increased risk of Coronary Heart Disease (CHD). The authors reported that the Conicity Index was the body composition marker best associated with increased CHD risk.

I enjoyed serving as a reviewer of this manuscript and think it is a very interesting topic. The authors pose a research question that is not really new, yet they use novel body composition markers such as the Body adiposity index, together with other classic well studied markers such as the body mass index, in a specific subpopulation as are the patients with type 2 diabetes mellitus. This may add useful information regarding the choice for a specific marker to be used in clinical practice and therefore may aim to contribute to more financial a time efficient clinical practice along with better assessment of risk in the specific subpopulation possibly enhancing the patients’ outcome. Nevertheless, after reading the paper, I found several methodological issues and other overlooked aspects that need to be addressed. I think this paper needs a throughout revision before it can be resubmitted.

Major compulsory revisions:

1- One major comment concerns the terminology used by the authors regarding body fat (BF) content and distribution, as mentioned in the second paragraph of the “Background”. First we recommend using the terminology proposed by Sardinha & Teixeira (1) that is a sound and consensual terminological benchmark. Accordingly BMI is used to quantify body mass related to height, not just body mass. Body mass is assessed by weight measurement. Also, not all body indexes used assess BF distribution. Waist circumference (WC), for example, is a predictor of central BF accumulation, therefore it is a predictor of regional BF and not BF distribution. Waist-to-height ratio (WHtR), as WC alone, is a marker of central BF accumulations, but in this case corrected for height. Body adiposity index (BAI) is a predictor of whole body adiposity and therefore it is also incorrect to mention it as a marker of BF distribution. The only studied body indexes that can be unarguably considered BF distribution markers are the
Waist-to-hip ratio (WHR) and the Conicity Index (C-index) because they assess the ratio between two quantifying measures (WC and hip or WC and body mass corrected for height, respectively), therefore these do not give a sense of BF quantity, as the previous indexes, but give a sense of BF distribution.

2- Another major comment regards the usage of the model for risk assessment from the United Kingdom Prospective Diabetes Study (UKPDS). To my knowledge this was a tool developed and validated in Europe with European subjects, particularly United Kingdom citizens. The authors should present a rational for the usage of this model in a South American sample either in the “Methods” if there are scientific rational to support this option, or at least a mention should be made in the “Limitations” paragraph. This raises another question which regards the subjects ethnicity. The authors mentioned that ethnicity was self-reported and the sample was constituted mostly by whites. Considering this study was carried out in Brazil one question arises: were they referring to Latin whites or Caucasian whites. Because many epidemiological studies usually distinguish between Whites, Latins, Asians and Blacks and find non-neglectable metabolic-related risk differences.

3- The cut off values used in the conversion of some body indexes into dichotomous categorical variables also seem to lack rational. The cut off values for BMI, WC, WHR and WHtR are well established in the literature and properly referenced in the paper. However the cutoff values chosen for the BAI and for de C-Index lack proper explanation and/or supportive references. The selection of the cut off values, particularly for the C-index may be influencing the results.

4- Considering the aim of this paper and the previous comment, I wonder why the authors didn’t use receiver operating characteristics (ROC) analysis. This would have allowed finding the best predictor of increased CHD risk and also the proper cutoff values for the studied sample.

5- The “Methods” section needs a full revision:

a. Only the equipment for Blood pressure is mentioned. The authors need to refer the instuments/equipments (model, brand and manufacturer) used in data collection and analysis. Including those used for anthropometric measurements, for blood collection and analysis.

b. Bibliographic references supporting the techniques and procedures are lacking. For example, the authors mention that WC was measured half distance between last rib and iliac crest, which seems like the WC measurement protocol endorsed by the World Health Organization (WHO), however the authors also mention the umbilicus which is not accounted by the mentioned WHO protocol. A bibliographic reference would have cleared this ambiguity. References are also lacking in other instruments/ techniques/ procedures described in the “Methods”: the Friedewald’s needs a reference; as do all laboratory measurements and anthropometric measurements. Many time there are modified versions of the same instruments and, without proper referencing, one cannot be sure which version of the instrument was used.
c. The authors mentioned a nutritional assessment but I could not find which instrument was used and therefore I could not replicate this assessment nor have a critical overview of it.

d. The Physical activity assessment was made using Kuopio Ischaemic Heart Disease Risk Factor Study 12-month Leisure-Time Physical Activity (LTPA) questionnaire, which has been used in subjects with type 2 diabetes (2). This questionnaire was adapted from the Minnesota Leisure Time Physical Activity Questionnaire (3) and was properly tested in the population of Eastern Finland (4, 5). The author mentioned that they adapted the questionnaire to «local habits». I wonder if this was validated and if the questionnaire is actually measuring what the authors claim it is. Physical activity is an important control variable and therefore this is not a minor issue.

6- Diabetes is a disease with a long time course and is mostly progressive in the damage it imposes to patients’ overall organs and health. I wonder why the authors didn’t accounted this variable as a control variable in the statistical analysis.

7- The discussion should be more deep and sound. There is an important, quite recent, study by Ashwell and colleagues (6) endorsing WHtR as the best body composition marker to assess cardiovascular risk, which is mentioned in the introduction section of this paper. Yet this study is not mentioned nor discussed in the discussion section of this paper. The discussion is much directed to C-index and overlooks the results obtained for the other variables. Authors were too concerned in leading the reader to the conclusion and did not show similar interest in understanding the results.

Minor essential revisions:
1- In the 2nd sentence of the “Background” section: it is not clear what you mean by «Although diabetes was once considered equivalent to coronary heart disease…»;

2- In the last sentence of the “Background” section the acronym UKPDS should be within the parenthesis and the fully written form should appear first in the text.

3- In the last sentence of the “Results” section is not clear what “its” refer to.

Discretionary revisions:
1- The first sentence of the “Results” section should be included in the “Methods” section, in the paragraph regarding the description of the sample;

2- Table 2 needs revision to enhance its’ readability:
   a. The normal level column can be removed and in the legend the authors can mentioned that normal level served as a reference;
   b. Tables’ first row need revision: normal levels, instead of levels normal… and so on.
c. Table could have a symbol to facilitate identification a visualization of significant results.

3- Data presented in figure 1 is better presented on a table.

References:


Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

No competing interests to disclose.