Reviewer's report

Title: The long-term coronary heart disease risk of previously obese patients with type 2 diabetes mellitus

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Reviewer: Altan Onat

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This study assesses the incident CHD risk of predominantly male Japanese diabetic patients (n=319) some of whom had been obese prior to being enrolled in a first visit to a hospital. Such maximal weight reported by patient (MAXBMI) was used in classifying the diabetic patients into 5 BMI categories. BMI at enrollment showed a similar increase though not being quite parallel to MAXBMI. Blood pressure, HbA1c, total, HDL- and LDL-cholesterol levels were similar across categories. Only never smoking and serum triglycerides tended to be non-significantly higher in the obese category, in addition to a significantly higher prevalence of diabetic retinopathy. While the CHD risk of the low 4 categories was similar in Kaplan-Meier analyses and multi-adjusted Cox model analyses, previously obese diabetic patients exhibited a roughly tripled risk of CHD (p=0.01) compared with the reference category.

This work of potential value has important limitations that need to be addressed.

1) Women constitute only one-quarter of the sample, and with only 49 cases of overall incident CHD, conclusions cannot apply but for men. This should be clearly stated.

2) Data provided in Table 1 may be considered scarce. No inflammation parameters (such as CRP, fibrinogen, or lipoprotein(a)) are available which are relevant with respect to obesity, diabetes and CHD. Sex distribution across categories needs to be given as also that of current smokers (rather than combining current with former smokers). Smoking categories in the multivariable Cox models should also better be grouped to 3.

3) Some information should be given on females whether –even if not significant-similar or divergent trends are observed.

4) The approximate time interval between reported MAXBMI and measured enrollment-BMI would be informative to state.

5) In view of a presumable threshold effect (rather than a graded increase) of BMI in all Cox models, interaction of an unrecognized factor with BMI needs to be put forward.

6) The difference between the two variables may be used as an independent variable in the Cox regression along with the adjusted risk factors in Model 2, to determine better whether previous obesity or rather preceding weight loss was the predictor of coronary risk.
7) The observation that diabetic retinopathy was related both to obesity and to CHD risk merits better commenting. In a total of 341 type-1 diabetic patients, compared with the remaining patients, proliferative diabetic retinopathy was found to be associated with increased levels of Lp(a) in whom apoA-I concentrations were insignificantly elevated as well (Guerci B, et al. Diabet Metabolism 1999; 25:412).

8) The Discussion is very brief; needs to be more in-depth. Authors may benefit from A. Onat et al. (Metabolism 2011; 60:499 and Acta Diabetol 2011 Jul 16 [Epub] ). The sentence “… metabolic memory of high glucose, dyslipidemia and hypertension before enrollment (Refs)” is vague and may be omitted. Lp(a) may likely be the critical element.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

No competing interest.