Reviewer's report

Title: The effect of endogenously released glucose, insulin, glucagon-like peptide 1, ghrelin on cardiac output, heart rate, stroke volume, and blood pressure

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Reviewer: amalia gastaldelli

Reviewer's report:

The article by Hlebowicz et al addresses a simple but important question that is related to the postprandial changes in blood flow, cardiac output and blood pressure. I found the article interesting for the implication in metabolic studies.

Major Compulsory Revisions

- The major comment is that the conclusion of the abstract is understating the message of this paper. Many metabolic studies have been recently carried out in postprandial state, also because GLP-1 and GIP hormone are released after a meal. Several studies have investigated the effect of GLP-1 agonist on heart function and this should be highlighted in the discussion of this paper.

- Circulatory models, ie based on blood flow and cardiac output, have been recently proposed to study postprandial metabolism. The assumption to use these models is that CO is constant throughout the experiment. This article clearly shows that this is not the case and thus those models should not be used to evaluate postprandial state.

- In the abstract “In men, the postprandial changes in glucose levels were positively correlated to systolic blood pressure, the GLP-1 levels to SV, the insulin levels to CO, and the ghrelin levels to HR. Was the correlation insulin-CO and ghrelin levels significant only in men or in the entire cohort? It is not clear. The correlation should be performed in the entire cohort as multiple regression by correcting per gender and BMI. These results should be better discussed and try to interpret the result of correlation.

- Glucose and insulin concentrations after the meal were not very high. Given that insulin stimulates blood flow and (see for example Autonomic and hemodynamic responses to insulin in lean and obese humans., Muscelli E, JCEM 1998) and affects autonomic control of cardiac function, you should discuss this issue, since different meal could have higher insulin responses.

- Page 10. “To our best knowledge, this is the first study to examine at the effect of endogenously released glucose, insulin, glucagon-like peptide 1, ghrelin levels on CO, SV, HR, systolic and diastolic blood pressure in both men and women” please eliminate glucose from this sentence since after a mixed meal glucose production is suppressed so the great part of glucose measured in the systemic blood is exogenous, so the authors do not look at “endogenously released
- Table 1 and results. What was the rational to measure the variable of table 1 at 0, 30 and 110 instead of 120min?

-Figure 1 Were the AUC of GLP-1 different in men and women?

Minor Essential Revisions
Was blood for GLP-1 assessment collected with DPP-IV inhibitor? This is crucial for the validity of the assay. Was GLP-1 measured using an in house method or a commercial kit?

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.