Reviewer’s report

Title: Assessment of endogenous insulin secretion in insulin treated diabetes predicts postprandial glucose and treatment response to prandial insulin

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Reviewer: Klaus-Dieter Kohnert

Reviewer’s report:

In this manuscript, the authors address the important issue of guiding insulin therapy by measurement of C-peptide as a marker of endogenous insulin secretion. They demonstrated in their cross-sectional study for the first time a significant relationship between C-peptide levels and the impact of prandial exogenous insulin administration. This is a beautiful piece of work.

I have only to recommend a few minor essential revisions:

Minor essential revisions

1. Methods
   - The authors note that participants fasted overnight without taking their morning insulin or OHAs. As far as sulfonylureas are concerned, for example glimepiride, it can not be expected that the effects of this agent tail off within a few hours after treatment discontinuation. Thus C-peptide levels prior to the MMT might be higher and C-peptide increments lower in these cases so that they fall into upper C-peptide tertiles. Was this taken into consideration? I recommend that the authors briefly consider this point in their discussion.

2. Results
   - In Table 1, diabetes duration should additionally be included, because it appears plausible that the longer the disease, as in tertile 1, the lower the C-peptide levels.
   - Furthermore, I recommend to indicate the proportion of patients with type 1 and type 2 diabetes within the tertiles.
   - It is not clear why 102 patients were recruited but data for only 80 are shown (Table 1 and 2).

3. Discussion
   - When interpreting the results, the authors should take into account that elevated endogenous insulin levels represent a compensatory response to insulin resistance. The observation that in those study participants with the highest endogenous insulin secretion prandial exogenous insulin had little effect despite similar insulin doses can best be explained by greater insulin resistance.

Discretionary Revisions

1. Results
It would be interesting to know the carbohydrate content of the participants’ home meal compared to the MMT.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

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

**Declaration of competing interests:**

I declare that I have no competing interests.