Response to the Need for Identifying Standardized Indices for Measuring Glucose Variability

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We thank Picconi and colleagues[1] for their valuable comments on our study.[2] They observe a lack of standardization for measurement of glycemic variability (GV) and suggest that there might be different outcomes with different GV measures. Furthermore, the authors suggest a possible confounding role for insulin secretagogues on GV and oxidative stress parameters.

The lack of standardization of GV measurement methods is a problem we had discussed.[3] This lack limits comparison between trials and we would highly support development of a consensus on, ideally, one measure. We agree that mean amplitude of glycemic excursions has several limitations: not measuring excursions smaller than the standard deviation as well as not taking the frequency of excursions into account. Therefore, our group has developed a new measure that we believe overcomes these limitations and has proven robust in diabetes[4] and intensive care unit populations[5]: mean absolute glucose change (MAG). This is a simple summation of all changes in glucose per unit of time and can be taken from self-monitored blood glucose profiles, blood glucoses, and continuous glucose monitoring traces.

To investigate the influence of different measurement methods, we also measured the relation between oxidative stress and continuous net glycemic action (reflected as CONGA-1, CONGA-2, CONGA-4) as well as mean of daily differences originally in the subject study.[2] As expected, all GV measures were highly correlated and, also for these additional measures, we were not able to show a correlation with oxidative stress in our population. To improve readability, we decided not to include them in the paper.

Picconi and colleagues suggest that our outcomes might have been influenced by insulin secretagogues and other drugs used in our study population. It could be that the formation of oxidative stress is prohibited by these medicaments but, as mentioned, our population showed optimal glycemic control. The results of our study therefore reflect the current situation of diabetes regulation, which relies on polypharmacy. Moreover, it is plausible that mean glucose is the main driver of oxidative stress[6] and not the way by which that mean glucose is reached. Noteworthy in this perspective is that the patients in the original Monnier article[7] were allowed to use insulin secretagogues, which did not seem to influence the positive correlation found between GV and oxidative stress.

In conclusion, we support that future studies use standardized GV measures, for which we propose the MAG, and, in case of isoprostane measurement, high-performance liquid chromatography tandem mass spectrometry to measure oxidative stress.

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Abbreviations: (CONGA) continuous net glucemic action, (GV) glucose variability, (MAG) mean absolute glucose change

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