RESPONSE TO COMMENT ON TAY ET AL.

A Very Low-Carbohydrate, Low–Saturated Fat Diet for Type 2 Diabetes Management: A Randomized Trial. Diabetes Care 2014;37:2909–2918

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Maiorino et al. (1) correctly identify that HbA_{1c} was the primary outcome of our previously reported study (2) but may have misunderstood the statistical approach used to evaluate the diet effects on outcomes, including HbA_{1c}, when they suggest a subgroup analysis was used as opposed to the whole-population analysis that was performed.

The primary objective of our study was to compare the effects of a very low-carbohydrate (LC) diet to a high–unrefined carbohydrate (HC) diet on glycemic control and cardiovascular disease risk factors in obese adults with type 2 diabetes. The study used a randomized groups, pretest-posttest design and the planned analysis of the outcomes was to use ANCOVA to test between-group differences at posttest assessments (week 24), with baseline and sex as covariates. ANCOVA confers greater statistical power compared with other approaches that compare change scores by correcting for regression to the mean (3,4).

For many statistical models, testing model assumptions prior to analysis is mandatory. In our study, comparisons of regression slopes (test of the interaction between the pretest data and the grouping variable) were conducted to determine whether the ANCOVA assumption of homogeneity of regression slopes was met. For outcomes such as HbA_{1c} this assumption was not met, indicating that the response of the outcome to the treatment is dependent on its baseline level. The significant interaction between diet and baseline HbA_{1c} also indicates that the main diet effect being requested by Maiorino et al. (1) is no longer a meaningful or useful term that can be interpreted independent of the baseline covariate. Consequently, it was necessary to use the Johnson-Neyman (J-N) procedure (5) as an appropriate alternative primary statistical approach for the a priori analysis to investigate the interaction term.

The J-N procedure is used to identify regions of significance along the observed range of the pretest measure where diet differences across the entire group on the posttest measures occur (i.e., where the diet groups differed). We emphasize that the J-N procedure represents an analysis of the whole population in a single statistical model to test the a priori hypothesis and is not a subgroup analysis. We further confirm that no data subanalyses were performed and that the smaller "subgroup" numbers reported were generated from the primary whole-group analysis performed with the J-N procedure.

We hope this explanation provides greater clarification that the HbA_{1c} results reported were analyzed as a whole-group population and the J-N procedure used appropriately provides the average reader with the relative merit of each diet on the primary outcome across a population with a wide spectrum of initial HbA_{1c} levels.

Importantly, the HbA_{1c} results need to be considered in conjunction with other study findings. Although the whole-group analysis revealed that an additional effect for the LC diet on HbA_{1c} may only be evident for patients with a baseline HbA_{1c} >7.8% (62 mmol/mol), the LC diet conferred greater advantages for reducing antiglycemic medication requirements and improving diurnal blood glucose stability across the entire study population examined, suggesting that it may confer advantages for optimizing glycemic control in type 2 diabetes.

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

References

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