COMMENTS AND RESPONSES

Comment on: Besser et al. Lessons From the Mixed-Meal Tolerance Test: Use of 90-Minute and Fasting C-Peptide in Pediatric Diabetes. Diabetes Care 2013;36:195–201

It was extremely gratifying to read an interesting article in *Diabetes Care* by Besser et al. (1) that suggested that 90-min C-peptide is a highly sensitive and specific measure of area under curve and peak C-peptide in children and adolescents with type 1 diabetes and offers a practical alternative to a full mixed-meal tolerance test. The authors also suggested that C-peptide measured at diagnosis and age at diagnosis can be used to predict the time taken for patients to become insulin-deficient. The authors suggested that those with the lowest tertile of fasting C-peptide (<0.17 nmol/L) reached insulin deficiency quicker than those in the highest tertile of fasting C-peptide (≥0.29 nmol/L) using the Kaplan-Meier method. Similarly, those diagnosed at a younger age (<10 years) became insulin-deficient faster than those diagnosed at an older age (>13 years).

We would like to point out that Kaplan-Meier graphs shown in the study to graphically represent the above findings did not begin from unity. When computing survival probability using the Kaplan-Meier method, each data table should begin with a survival time of zero, even though no subject actually failed at the start of follow-up. The reason for this to allow for the possibility that some subjects might have been censored before the earliest failure time. So the probability of surviving past zero is unity, as it will always be for any dataset (2).

Similarly, Besser et al. used the same curve plots to compare which subset of patients became insulin-deficient earlier using "fasting C-peptide at times of diagnosis versus time" and "age at diagnosis versus time" as variables. Since the starting points of these curves are different, as apparent from the given figures, the curves cannot be compared to predict which group became insulin-deficient earlier. Patients that have a starting point at a lower level in the graph will become insulin-deficient earlier because they have less insulin reserve at the start. It would be a pleasure if the authors could provide us with data regarding the difference in rate of fall of insulin with time in different groups and analyze the difference, if any.

Further, we would like to point out that the Kaplan-Meier curve for group 1 is consistently higher than the ones for group 2 and group 3, and as the number of weeks increase, the three curves appear to get farther apart, indicating group 1 had better survival prognosis. But to compare three or more survival curves, the log-rank test should be used. The null hypothesis for this more general situation is that "all survival curves are the same." The log-rank test is a large-sample χ^2 test that uses as its test criterion a statistic that provides an overall comparison of the Kaplan-Meier curves being compared (3). It would be a pleasure if the authors could provide us with data regarding this.

SANDEEP CHAUDHARY, MD
ANUBHAV THUKRAL, MD
MANOJ KATARIA, MD
SUJOY GHOSH, DM, FRCP (EDIN)
SATINATH MUKHERJEE, DM
SUBHANKAR CHOWDHURY, DM

From the Department of Endocrinology, Institute of Post Graduate Medical Education and Research, Seth Sukhlal Karnani Memorial Hospital, Kolkata, West Bengal, India.
Corresponding author: Anubhav Thukral, anubhavthukral@rediffmail.com.
DOI: 10.2337/dc13-0369

Acknowledgments—No potential conflicts of interest relevant to this article were reported.

References

1. Besser REJ, Shields BM, Casas R, Hattersley AT, Ludvigsson J. Lessons from the mixed-meal tolerance test: use of 90-minute and fasting C-peptide in pediatric diabetes. Diabetes Care 2013;36:195–201
2. Kleinbaum DG, Klein M. Kaplan-Meier survival curves and the log-rank test. In *Survival Analysis: A Self-Learning Text*. 2nd ed. New York, Springer-Verlag, 2005, p. 52
3. Kleinbaum DG, Klein M. Kaplan-Meier survival curves and the log-rank test. In *Survival Analysis: A Self-Learning Text*. 2nd ed. New York, Springer-Verlag, 2005, p. 57–61