Journal of Diabetes Science and Technology
2024, Vol. 18(2) 528–529

DOI: 10.1177/19322968231220064
journals.sagepub.com/home/dst
Sage

Response to Sensitivity of the Glycemia Risk Index to Effects of Automated Insulin Delivery Initiation

David C. Klonoff, MD, FACP, FRCP (Edin), Fellow AIMBE[1], Michael A. Kohn, MD, MPP[2], David Rodbard, MD[3], Rachel E. Aaron, BA[4], and Tiffany Tian, BA[4]

Keywords
automated insulin delivery, continuous glucose monitor, diabetes, glycemia risk index, time in range

Donaldson et al[1] summarized glycemic results for a real-world population initiated on automated insulin delivery (AID) systems and previously reported in greater detail.[2] At 12 months, the Glycemia Risk Index (GRI) improved by 8.7 percentiles, and time in range ($TIR^{70\text{-}180\ mg/dL}$) improved by 8.1%. The GRI is calculated as the quality of glycemia based on a hypoglycemia component and a hyperglycemia component. In Donaldson's population, following AID use, the improvement in the GRI was limited to a reduced hyperglycemia component (reflecting less time in hyperglycemia), whereas the hypoglycemia component remained unchanged (reflecting no change in time in hypoglycemia).[1]

This was an unusual patient cohort with a low average rate of time below range ($TBR_{<70\ mg/dL}$) of only 1.3% at onset of AID treatment.[2] This low incidence of hypoglycemia did not change from the intervention. By contrast, in the Wireless Innovation for Seniors with Diabetes Mellitus Randomized Controlled Trial (WISDM RCT) of people with type 1 diabetes (PWT1D), the mean pre-intervention $TBR^{70\text{-}180\ mg/dL}$ was 5%.[3] In the Diabeloop study on PWT1D, an AID system resulted in TBR reduction from 2.4% to 1.3%,[4] which is the same level as the pretreatment $TBR^{70\text{-}180\ mg/dL}$ of the Donaldson cohort.[2] Donaldson's real-world cohort had a baseline %CV of 34%,[2] which is consistent with "stable glucose levels" (defined as <36%) in the 2019 international consensus statement on continuous glucose monitoring (CGM).[5]

As Donaldson's team demonstrated, in a population with a low frequency of hypoglycemia and stable glucose levels, an intervention not affecting the population's minimal baseline hypoglycemia is unlikely to benefit GRI much more than TIR. They reported that the improvement in GRI exceeded the improvement in TIR at both time periods where these investigators compared the two metrics (delta GRI in percentiles vs delta TIR in percent at 13[1] vs 11[2] at 1 month and 8.7[1] vs 8.1[1] at 12 months). The effect of treatment (AID initiation in the Donaldson series) depends not only on the treatment but on the baseline characteristics of the group being treated.

The GRI was developed to reflect both hypoglycemia and hyperglycemia. If there is no overall change in hypoglycemia, then the overall hypoglycemia component of the GRI should not change. Reducing severe (Level 2) hyperglycemia (glucose > 250 mg/dL) can reduce the GRI substantially, but if improvements are limited to reducing mild (Level 1) hyperglycemia (glucose > 180-250 mg/dL), then the hyperglycemia component of the GRI should decrease less.[6] Donaldson's report did not separate time above range into time in mild hyperglycemia and time in severe hyperglycemia.[1,2] In a study population with a higher frequency of hypoglycemia or greater glycemic variability than Donaldson's, the difference between improvement in GRI and TIR would be more impressive.

We agree with Donaldson's team's conclusion that evaluating GRI in cohorts with higher baseline rates of hypoglycemia following initiation of diabetes interventions would further assist with evaluating the clinical utility of GRI. When an intervention is administered to a population with larger baseline risks for hypoglycemia or greater baseline glycemic variability than Donaldson's, GRI would be expected to show greater sensitivity than $TIR^{70\text{-}180\ mg/dL}$.

[1]Diabetes Research Institute, Mills-Peninsula Medical Center, San Mateo, CA, USA
[2]University of California, San Francisco, San Francisco, CA, USA
[3]Biomedical Informatics Consultants LLC, Potomac, MD, USA
[4]Diabetes Technology Society, Burlingame, CA, USA

Corresponding Author:
David C. Klonoff, MD, FACP, FRCP (Edin), Fellow AIMBE, Diabetes Research Institute, Mills-Peninsula Medical Center, 100 South San Mateo Drive, Room 5147, San Mateo, CA 94401, USA.
Email: dklonoff@diabetestechnology.org

Abbreviations

AID, automated insulin delivery; GRI, Glycemia Risk Index; PWT1D, people with type 1 diabetes; TBR, time below range; TIR, time in range

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: DCK is a consultant for Afon, Better Therapeutics, Integrity, Lifecare, Nevro, Novo, and Thirdwayv. DR is a consultant to Eli Lilly & Co. Inc. and Better Therapeutics, Inc. He has previously provided consulting services to multiple companies and organizations developing glucose meters, continuous glucose monitors, insulin pumps, digital connected insulin pens, and systems for automated insulin delivery, data analytics, clinical decision support, and other technologies to assist in the medical management of people with diabetes. The remaining authors have nothing to disclose.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

ORCID iDs

David C. Klonoff https://orcid.org/0000-0001-6394-6862
Michael A. Kohn https://orcid.org/0000-0001-5459-5044
David Rodbard https://orcid.org/0000-0002-5547-3564
Rachel E. Aaron https://orcid.org/0009-0005-5120-2264
Tiffany Tian https://orcid.org/0009-0003-1417-6445

References

1. Donaldson LE, Vogrin S, McAuley SA. Sensitivity of the glycemia risk index to effects of automated insulin delivery initiation [Published online ahead of print November 6, 2023]. *J Diabetes Sci Technol*. doi:10.1177/19322968231208957.
2. Donaldson LE, Fourlanos S, Vogrin S, MacIsaac RJ, Colman PG, McAuley SA. Automated insulin delivery among adults with type 1 diabetes for up to 2 years: a real-world, multicentre study [Published online ahead of print June 16, 2023]. *Int Med J*. doi:10.1111/imj.16143.
3. Miller KM, Kanapka LG, Rickels MR, et al. Benefit of continuous glucose monitoring in reducing hypoglycemia is sustained through 12 months of use among older adults with type 1 diabetes. *Diabetes Technol Ther*. 2022;24(6):424-434. doi:10.1089/dia.2021.0503.
4. Amadou C, Franc S, Benhamou PY, et al. Diabeloop DBLG1 closed-loop system enables patients with type 1 diabetes to significantly improve their glycemic control in real-life situations without serious adverse events: 6-month follow-up. *Diabetes Care*. 2021;44(3):844-846. doi:10.2337/dc20-1809.
5. Battelino T, Danne T, Bergenstal RM, et al. Clinical targets for continuous glucose monitoring data interpretation: recommendations from the international consensus on time in range. *Diabetes Care*. 2019;42(8):1593-1603. doi:10.2337/dci19-0028.
6. Klonoff DC, Wang J, Rodbard D, et al. A Glycemia Risk Index (GRI) of hypoglycemia and hyperglycemia for continuous glucose monitoring validated by clinician ratings [Published online ahead of print March 29, 2022]. *J Diabetes Sci Technol*. doi:10.1177/19322968221085273.