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Comparable Glycemic Risk Index (GRI) with Inhaled Insulin and Usual Care in Adults with Type 1 Diabetes (INHALE-3)

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INTRODUCTION

Glycemic Risk Index (GRI) is a recently described single metric that integrates continuous glucose monitoring (CGM) derived hyperglycemia and hypoglycemia exposure to quantify overall glycemic risk, which has been shown to correspond closely to clinician risk rankings of overall quality of glycemia. The GRI methodology was applied to the INHALE-3 trial, which evaluated adults with type 1 diabetes who were randomized to inhaled Technosphere Insulin (TI) versus continuation of their usual care (UC) regimen after 17 weeks of treatment.

AIM

To evaluate overall GRI between TI and rapid-acting insulin analogs (RAA) after 17 weeks of treatment in adults with Type 1 diabetes from the INHALE-3 trial.

METHODS

- GRI was calculated per Klonoff et al. (2022) using INHALE-3 CGM-derived level 1 and level 2 hypoglycemia and hyperglycemia data from the two weeks preceding the 17-week visit.
- Participants in TI and UC arms were categorized into Zones A - E, representing progressively higher risk.
- Subgroups were analyzed based on starting insulin regimen, including (1) multiple daily injections (MDI) or sensor-augmented pumps (SAP) and (2) automated insulin delivery (AID).

RESULTS

- Among all 111 participants with CGM data at week 17 (TI N=55, UC N=56), mean (SD) GRI was 55.9 ± 26.1 for TI and 59.1 ± 22.9 for UC. No statistically significant difference was observed between groups (p=0.502).
- Zone analysis showed numerically more TI users in Zone A (lowest risk) versus UC (n=6 vs. n=2). The distribution in higher-risk zones (D and E) was similar between treatment groups.
- Subgroup analysis of participants who started the study on MDI/SAP therapy and switched to TI (N=29), compared to staying on MDI/SAP (UC, N=27) demonstrated a significantly lower GRI at Week 17 with TI (55.0 ± 22.7) compared to UC (70.9 ± 20.4) (p=0.0079). Subgroup analysis of AID therapy GRI was similar between groups (p=0.146).

Figure 1. Glycemic Risk Index Grid, INHALE-3 TI and UC

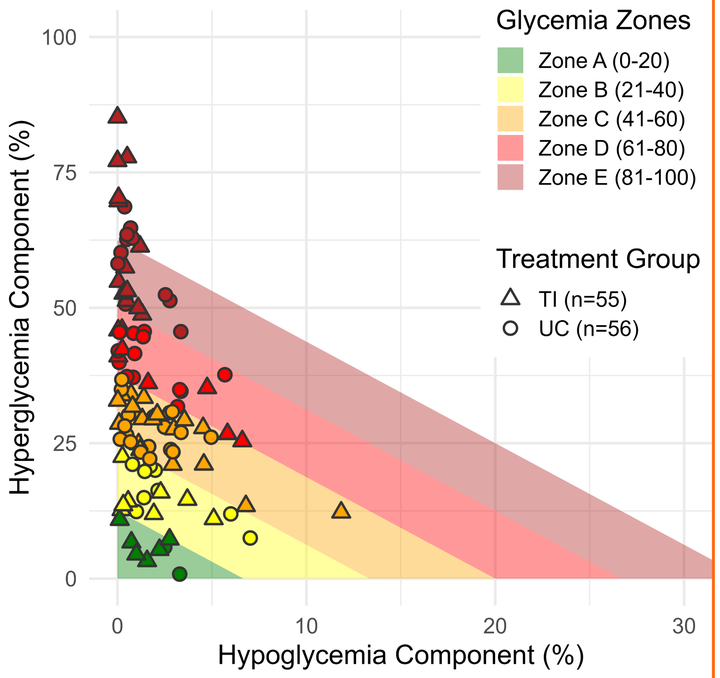

Table 1. Glycemic Risk Zone Distribution, INHALE-3 TI and UC

	Zone A (0-20)	Zone B (21-40)	Zone C (41-60)	Zone D (61-80)	Zone E (81-100)
TI	6 (11%)	8 (15%)	20 (36%)	8 (15%)	13 (24%)
UC	2 (4%)	9 (16%)	20 (36%)	14 (25%)	11 (20%)

CONCLUSIONS

The GRI metric provides a new perspective on glycemic risk in addition to traditional metabolic measures, which may be more sensitive to identifying patient risks corresponding with clinician risk rankings.

Overall, GRI in the INHALE-3 study was comparable between TI and UC, consistent with CGM and HbA1c outcomes reported previously, further supporting TI as an option for adults with Type 1 diabetes.

Although not different overall, the greater proportion of TI users in Zone A compared with UC may suggest a potential advantage for reducing glycemia risk with TI.

TI demonstrated significantly lower GRI than UC in the MDI/SAP subgroup, indicating that TI may have unique advantages to reducing glycemia risk for patients using those regimens. In the AID subgroup, outcomes were not significantly different between TI and UC, indicating TI may be comparable to AID in terms of glycemia risk.

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