Variability of insulin sensitivity for diabetics and non-diabetics during the first 3 days of ICU stay

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Introduction: Safe, effective tight glycemic control (TGC) can improve outcomes, but is difficult to achieve consistently. Glycemic level and variability, particularly early in a patient's stay, are a function of variability in insulin sensitivity/resistance resulting from the level and evolution of stress response, and are independently associated with mortality.

Objectives: To examine the daily evolution of variability of insulin sensitivity in ICU patients, and determine if critically ill diabetic patients display different metabolic levels or variability.

Method: Retrospective analysis of patient data (N=257 patients, 26201hours) from the SPRINT TGC study where SPRINT was commenced within 12 hours of ICU admission. Model-based insulin sensitivity (SI) was identified each hour and hour-to-hour percent changes in SI were assessed for days 1-3 individually and day 4 onward. Diagnosed (T1DM and T2DM) diabetics (N=59) are compared to non-diabetic patients (N=198) on both cohort and per-patient bases to assess differences in metabolic level or variability. Cumulative distribution functions, median values, and 90% range (5^{th}-95th percentiles) are used to assess differences between groups and their evolution over time.

Results: In both diabetic and non-diabetic groups, SI increases significantly over the first 24 hours ($p<0.02$). For days 2-3, further increases are not clinically or statistically significant. However, median insulin sensitivity is 18-42% lower for diabetics compared to non-diabetics over days 1-3 and 4 onward ($p<0.05$).

SI Variability (hour-to-hour percentage change) is higher on day 1 than days 2, 3 and 4 onward ($p<0.0001$) for both diabetic and non-diabetic groups. SI variability decreases during days 2-3, but the reduction is much smaller and not clinically or statistically significant. Diabetics are significantly more variable than non-diabetics on days 1-3 of ICU stay ($p<0.05$).

Conclusion: ICU patients have lower insulin sensitivity and are more variable on day 1 of stay compared to days 2-3 and 4 onward. Diabetic patients have even lower and more variable SI compared to non-diabetics during days 1-3. Greater variability with lower SI early in a patient's stay greatly increases the insulin required, potential glucose flux due to variation in SI, and thus the risk of greater glycemic variability and hypoglycemia – all of which reduce potential positive outcomes. Clinically, these results suggest that TGC patients, particularly those with a diabetic history, will require greater measurement frequency, reduced reliance on insulin, and more explicit specification of carbohydrate nutrition in Days 1-3 to safely minimize outcome glycemic variability.