Variability of insulin sensitivity during the first 4 days of critical illness

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Introduction:
Safe, effective tight glycaemic control (TGC) can improve outcomes in critical care patients, but is difficult to achieve consistently. Insulin sensitivity defines the metabolic balance between insulin concentration and insulin mediated glucose disposal. Hence, variability of insulin sensitivity can cause variable glycaemia. This study investigates the daily evolution of model-based insulin sensitivity level and variability for critical care patients receiving TGC during the first four days of their ICU stay.

Methods:
This study is a retrospective analysis of patient data (N=164 patients, 12067 hours) from the SPRINT TGC study in the Christchurch Hospital ICU [1]. All patients commenced TGC within 12 hours of ICU admission and spent at least 24 hours on the SPRINT protocol.

Model-based insulin sensitivity (*SI*) was identified using a validated glucose-insulin system model developed for critical care patients [2]. *SI* was identified every hour for each patient using clinical data and the model. Absolute level and hour-to-hour percent changes in *SI* were assessed on cohort and per-patient bases. Levels and variability of *SI* were compared over time on 24-hour and 6-hour timescales for the first 4 days of ICU stay.

Results:
Cohort and per-patient median *SI* levels increased by 34% and 33% ($p<0.001$) between days 1 and 2 of ICU stay. Concomitantly, cohort and per-patient *SI* variability reduced by 32% and 36% ($p<0.001$). For 72% of the cohort, median *SI* on day 2 was higher than day 1. The day 1-2 results were the only clear, statistically significant trends across both analyses.

Analysis of the first 24 hours using 6-hour blocks of *SI* data showed that most of the improvement in insulin sensitivity level and variability seen between days 1 and 2 occurred during the first 12-18 hours of day 1. This rapid improvement was likely due to the decline of counter-regulatory hormones as the acute phase of critical illness progressed.

Conclusions:
ICU patients have significantly lower and more variable insulin sensitivity on day 1 than later in their ICU stay and particularly during the first 12 hours. Clinically, these results suggest that while using TGC protocols with patients during their first few days of ICU stay, extra care should be afforded. Increased measurement frequency, higher target glycaemic bands, conservative insulin dosing and modulation of carbohydrate nutrition should be considered to safely minimize outcome glycaemic variability and reduce the risk of hypoglycaemia.

References:
1. Chase, J.G. et al.: Critical Care 2008; 12: R49
2. Lin, J. et al.: Comp. Methods Programs Biomed. 2011; 102: 192-205