

Safety and Performance of Stochastic Targeted (STAR) Glycemic Control of Insulin and Nutrition – First Pilot Results

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Introduction: Tight glycemic control (TGC) has shown benefits but been difficult to achieve consistently. STAR (Stochastic TARgeted) is a flexible, model-based TGC approach that directly accounts for intra- and inter- patient variability with a stochastically derived maximum 5% risk of blood glucose (BG) below 72mg/dL.

Objectives: To assess the safety, efficacy and clinical burden of a STAR TGC controller modulating both insulin and nutrition inputs in pilot trials.

Method: Seven patients covering 660 hours. Insulin and nutrition interventions are given 1-3 hourly as chosen by the nurse to allow them to manage workload. Interventions are designed to maximize the overlap of the model-predicted (5-95th percentile) range of BG outcomes with the 4.0-6.5mmol/L band, and thus guarantee a maximum 5% risk of BG<4.0mmol/L..

All measurements were taken with bedside glucometers. Interventions are calculated using clinically validated computer models of human metabolism and its variability in critical illness. Carbohydrate intake (all sources) was selected to maximize intake up to 100% of SCCM/ACCP goal (25kg/kcal/hour). Insulin doses were limited (8U/hour maximum), with limited increases based on current rate (0.5-2.0U/hour).

For context, BG results are compared to those for the SPRINT TGC cohort at the same hospital (current standard of care), which reduced mortality 25-40% for LoS≥3days.

Written informed consent was obtained for all patients, approval was granted by the NZ Upper South A Regional Ethics Committee.

Results: 402 measurements were taken over 660 hours (1.65 hourly or 14.5/day), as nurses showed a preference for 2-hourly measurements (<10 3 hours intervals chosen). Median [IQR] cohort BG was 5.9 [5.2-6.8]mmol/L. Overall, 63.2%, 75.9% and 89.8% of measurements were in the 4.0-6.5mmol/L, 4.0-7.0mmol/L and 4.0-8.0mmol/L bands. There were no hypoglycemic events (BG<2.2mmol/L) and the minimum recorded BG was 3.5mmol/L with 4.5% <4.0mmol/L. Only 0.2% (1 measurement) exceeded 10.0mmol/L.

Per-Patient the median [IQR] hours of TGC was 92 [29-113]hours using 53 [19-62] measurements (median: ~13.5 measurements/day). Median [IQR] per-patient results were: BG, 5.9 [5.8-6.3]mmol/L; Carbohydrate Administered, 6.8 [5.5-8.7]g/hour (~70% goal feed median using low CHO enteral nutrition); Insulin Administered, 2.5 [0.1-5.1]U/hour. All patients achieved BG<6.1mmol/L.

For comparison, the SPRINT cohort BG was 5.7 [5.0-6.6]mmol/L, and per-patient median BG was 5.8 [5.3-6.4]mmol/L, with a 2% (by patient) rate of hypoglycemia.

Conclusion: STAR TGC modulating insulin and nutrition inputs provided very tight control with minimal variability by managing intra- and inter- patient variability. Performance and safety exceed that of SPRINT, which reduced mortality and cost in the Christchurch ICU. The use of

glucometers did not appear to impact the quality of TGC. Finally, clinical workload was self-managed and reduced 20% compared to SPRINT.