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ORIGINAL ARTICLE

Stochastic Targeted (STAR) Glycemic Control: Design, Safety, and Performance

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Abstract

Introduction:

Tight glycemic control (TGC) has shown benefits but has been difficult to achieve consistently. STAR (Stochastic TARgeted) is a flexible, model-based TGC approach that directly accounts for intra- and interpatient variability with a stochastically derived maximum 5% risk of blood glucose (BG) below 72 mg/dl. This research assesses the safety, efficacy, and clinical burden of a STAR TGC controller modulating both insulin and nutrition inputs in virtual and clinical pilot trials.

Methods:

Clinically validated virtual trials using data from 370 patients in the SPRINT (Specialized Relative Insulin and Nutrition Titration) study were used to design the STAR protocol and test its safety, performance, and required clinical effort prior to clinical pilot trials. Insulin and nutrition interventions were given every 1–3 h as chosen by the nurse to allow them to manage workload.

Interventions were designed to maximize the overlap of the model-predicted (5–95th percentile) range of BG outcomes with the 72–117 mg/dl band and thus provide a maximum 5% risk of BG <72 mg/dl. Interventions were 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 the American College of Chest Physicians/Society of Critical Care Medicine (ACCP/SCCM) goal (25 kg/kcal/h). Insulin doses were limited (8 U/h maximum), with limited increases based on current rate (0.5–2.0 U/h). Initial clinical pilot trials involved 3 patients covering ~450 h. Approval was granted by the Upper South A Regional Ethics Committee.

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Abbreviations: (APACHE II) Acute Physiology and Chronic Health Evaluation II, (ACCP) American College of Chest Physicians, (CDF) cumulative distribution function, (EN) enteral, (ICU) intensive care unit, (IQR) interquartile range, (LoS) length of stay, (PN) parenteral, (SCCM) Society of Critical Care Medicine, (SPRINT) Specialized Relative Insulin Nutrition Titration, (STAR) Stochastic TARgeted, (TGC) tight glycemic control

Keywords: critical care, glycemic control, ICU, intensive care, intensive insulin therapy, SPRINT, STAR, stochastic, targeted, TGC

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Abstract cont.

Results:

Virtual trials indicate that STAR provides similar glycemic control performance to SPRINT with 2–3 h (maximum) measurement intervals. Time in the 72–126 mg/dl and 72–145 mg/dl bands was equivalent for all controllers, indicating that glycemic outcome differences between protocols were only shifted in this range. Safety from hypoglycemia was improved. Importantly, STAR using 2–3 h (maximum) intervention intervals reduced clinical burden up to 30%, which is clinically very significant. Initial clinical trials showed glycemic performance, safety, and management of inter- and intrapatient variability that matched or exceeded the virtual trial results.

Conclusions:

In virtual trials, STAR TGC provided tight control that maximized the likelihood of BG in a clinically specified glycemic band and reduced hypoglycemia with a maximum 5% (or lower) expected risk of light hypoglycemia (BG <72 mg/dl) via model-based management of intra- and interpatient variability. Clinical workload was self-managed and reduced up to 30% compared with SPRINT. Initial pilot clinical trials matched or exceeded these virtual results.

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