Hypoglycemia Detection in Critical Care Using Continuous Glucose Monitors: An *in Silico* Proof of Concept Analysis

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Abstract

Background:

Tight glycemic control (TGC) in critical care has shown distinct benefits but has also been proven difficult to obtain. The risk of severe hypoglycemia (<40 mg/dl) has been increased significantly in several, but not all, studies, raising significant concerns for safety. Continuous glucose monitors (CGMs) offer frequent measurement and thus the possibility of using them for early detection alarms to prevent hypoglycemia.

Methods:

This study used retrospective clinical data from the Specialized Relative Insulin Nutrition Titration TGC study covering seven patients who experienced severe hypoglycemic events. Clinically validated metabolic system models were used to recreate a continuous blood glucose profile. *In silico* analysis was enabled by using a conservative single Gaussian noise model based on reported CGM clinical data from a critical care study [mean absolute percent error (MAPE) 17.4%]. A novel median filter was implemented and further smoothed with a least mean squares-fitted polynomial to reduce sensor noise. Two alarm approaches were compared. An integral-based method is presented that examined the area between a preset threshold and filtered simulated CGM data. An alarm was raised when this value became too low. A simple glycemic threshold method was also used for comparison. To account for random noise skewing the results, each patient record was Monte Carlo simulated 100 times with a different random noise profile for a total of 700 runs. Different alarm thresholds were analyzed parametrically. Results are reported in terms of detection time before the clinically measured event and any false alarms. These retrospective clinical data were used with approval from the New Zealand South Island Regional Ethics Committee.

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Abstract cont.

Results:

The median filter reduced MAPE from 17.4% [standard deviation (SD) 13%] to 9.3% (SD 7%) over the cohort. For the integral-based alarm, median per-patient detection times ranged, t, from –35 minutes (before event) to –170 minutes, with zero to two false alarms per patient over the cohort and different alarm parameters. For a simple glycemic threshold alarm (three consecutive values below threshold), median per-patient alarm times were –10 to –75 minutes and false alarms were zero to seven; however, in one case, five of seven subjects never alarmed at all, despite the hypoglycemic event.

Conclusions:

A retrospective study used clinical hypoglycemic events from a TGC study to develop and analyze an integral-based hypoglycemia alarm for use in critical care TGC studies. The integral-based approach was accurate, provided significant lead time before a hypoglycemic event, alarmed at higher glycemic levels, was robust to sensor noise, and had minimal false alarms. The approach is readily generalizable to similar scenarios, and results would justify a pilot clinical trial to verify this study.

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