WHAT MAKES TGC PROTOCOLS "T" (TIGHT)? AN ANALYSIS OF DATA FROM 2 STUDIES


INTRODUCTION

Critically ill patients experience stress-induced hyperglycemia and high levels of insulin resistance. The occurrence of hyperglycemia, particularly severe hyperglycemia, is associated with increased morbidity and mortality. However, any tight glycemic control (TGC) result has to be viewed in the context of:

- Patient condition and cohort
- Levels and dosing of insulin and nutrition relative to glycemic levels (i.e. the protocol)
- Adaptability of the protocol to acute changes in patient condition.

The goal is to uncover aspects of successful tight glycemic control and delineate any differences in cohort that might require a less general, hospital/region-specific approach to tight glycemic control.

MODELS

Insulin sensitivity was fitted to retrospective data from glucose control under each protocol (SPRINT and Glucontrol). Model-based insulin sensitivity provides a measure of overall patient response to exogenous insulin and can indicate level of glycemic response and overall clinical condition.

Stochastic modelling is used to construct distributions from the model-identified insulin sensitivity (S(t)) profiles, which define the variability in S(t) and thus patient condition for each house of glucose control.

\[
\hat{G} = - \frac{\partial G}{\partial S} + S(t) \quad \frac{\partial S}{\partial t} + \frac{\partial G}{\partial t} + \frac{\partial G}{\partial S} \quad \frac{\partial S}{\partial t}
\]

\[
Q = K + \frac{\partial Q}{\partial t}
\]

\[
l = \frac{\partial l}{\partial t} + \frac{\partial l}{\partial S} \quad \frac{\partial l}{\partial t} \quad \frac{\partial l}{\partial S}
\]

METHODS

Comparisons of glycemic control with published studies often rely on comparing summary data presented in literature. The Glucontrol and SPRINT studies represent two completely independently designed and implemented protocols. Clinical data and model-based information from both studies are compared.

RESULTS AND DISCUSSION

Comparison of Glucontrol and SPRINT cohorts

<table>
<thead>
<tr>
<th>Glucontrol</th>
<th>SPRINT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>142</td>
</tr>
<tr>
<td>Male (%)</td>
<td>60.8</td>
</tr>
<tr>
<td>Apache II score median [IQR]</td>
<td>17 [14 - 22]</td>
</tr>
<tr>
<td>Hours of control</td>
<td>16,831</td>
</tr>
<tr>
<td>Total BG measurements</td>
<td>4,271</td>
</tr>
<tr>
<td>Median BG [mmol/L]</td>
<td>6.5 [3.7 - 7.4]</td>
</tr>
<tr>
<td>Insulin target [mmol/L]</td>
<td>20.0 [15.3 - 20.6]</td>
</tr>
<tr>
<td>Feed rate [mmol/L]</td>
<td>0.20 [0.10 - 0.30]</td>
</tr>
<tr>
<td>Percentage of measurement less than 4.4 mmol/L (%)</td>
<td>0.40</td>
</tr>
<tr>
<td>Percentage of measurement less than 2.2 mmol/L (%)</td>
<td>0.7</td>
</tr>
<tr>
<td>Percentage of measurement between 4.4 and 6.1 mmol/L (%)</td>
<td>3.0</td>
</tr>
</tbody>
</table>

• The Glucontrol cohort had higher insulin sensitivity at all likelihoods and for all observed percentiles compared to the SPRINT cohort.

• Stochastic modelling shows similar distributions of variability in S(t).

• So, S(t) is different but evolves similarly over time. Patient variability is a constant?

• The Moral: All things in moderation and balance

• The Technical Moral: You must know your nutrition to minimise the outcome BG variability (and patient variation)

• An Idea: Is unknown, variable nutrition protocols a cause of variable outcomes in multicentre trials?

COHORT SELECTION

- Leige, Belgium
- 350 patients
- Requires current and previous BG and prior insulin bolus size.
- 1-4 hour BG measurement interval
- Insulin delivered via infusion
- BG targets: 4.4 to 6.1 mmol/L

- Christchurch, New Zealand
- 393 patients
- Uses current and previous BG, current feed rate and prior insulin bolus size.
- 1-2 hour BG measurement interval
- Insulin delivered via bolus, maximum of 6U/hr
- BG target: 4.4 to 6.1 mmol/L

- The Technical Moral: You must know your nutrition to minimise the outcome BG variability (and patient variation)

- An Idea: Is unknown, variable nutrition protocols a cause of variable outcomes in multicentre trials?