Pancreatic Insulin Secretion in Critically Ill Patients

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Objective

- Glucose-insulin pharmacokinetic-pharmacodynamic (PK-PD) models can be used for improved glycemic control of critically ill patients.
- A key component of glucose-insulin PK-PD models is pancreatic insulin secretion.
- There is limited data in the literature quantifying insulin secretion in critically ill patients at physiologic levels.
- **Using prospectively collected data, this study creates a model of pancreatic insulin secretion in critically ill patients to improve glucose-insulin system modeling.**

Subjects

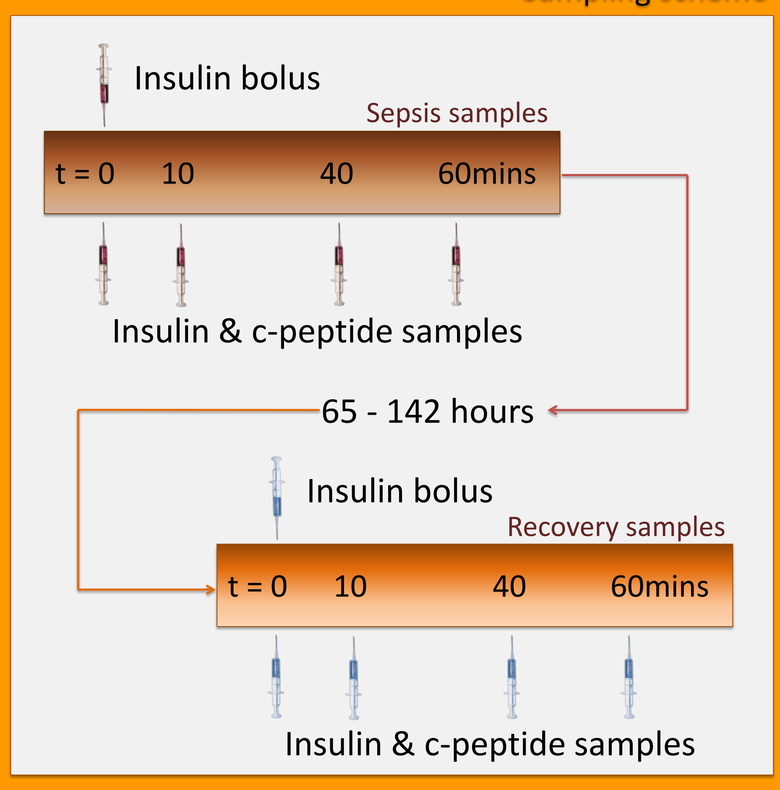
- 19 patients from the Christchurch Hospital ICU enrolled in a prospective clinical trial studying sepsis.
- Patients were included in the study if they met all of the following criteria:
  - ✓ Age ≥ 16 years.
  - ✓ Expected survival ≥ 72 hours.
  - ✓ Expected ICU length of stay ≥ 48 hours.
  - ✓ Entry to the SPRINT TGC protocol.
  - ✓ Suspected sepsis or SIRS score ≥ 3.
- No diagnosed Type I diabetic patients were included.

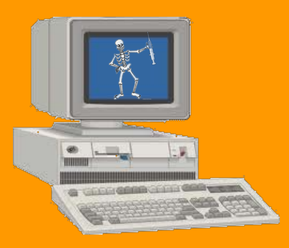
N	19
Age (years)	68 [57-75]
Gender (M/F)	10/9
APACHE II score	22.0 [18.3-26.8]
Confirmed sepsis	79%
Hospital mortality (L/D)	13/6
Diagnosed T2DM	3

Samples

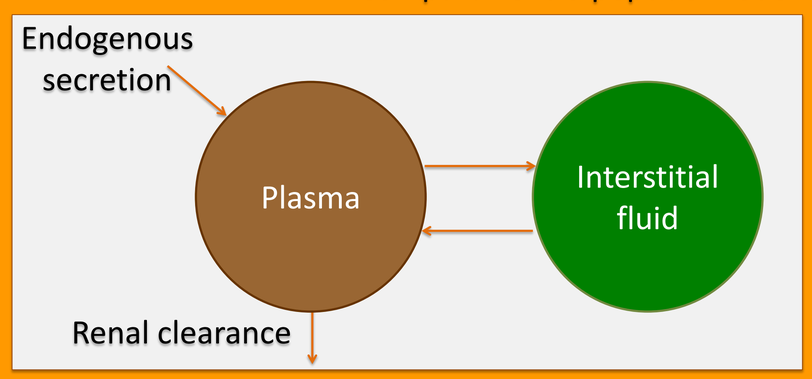
- Each patient had two sets of arterial blood samples taken, where each set consisted of 4 separate samples.
  - ✓ The first set of samples was taken at the commencement of the SPRINT TGC protocol.
  - ✓ The second set was taken when the patient consistently met less than 2 of the SIRS criteria
- Insulin and C-peptide concentrations were determined using immunometric assays.
- Blood glucose levels were measured with a bedside glucometer at t = 0 and t = 60 mins as per normal clinical practise.

Sampling scheme





2-compartment C-peptide model



Methods

- Pancreatic insulin secretion rates were deconvolved from C-peptide data using the model and population constants of van Cauter et al.
- Data from literature suggested a maximum secretion rate of 16U/hr.
- A minimum rate of 1U/hr was also adopted.
- Model fitting was performed by minimising the sum of the geometric means of the squared deviations in each dimension

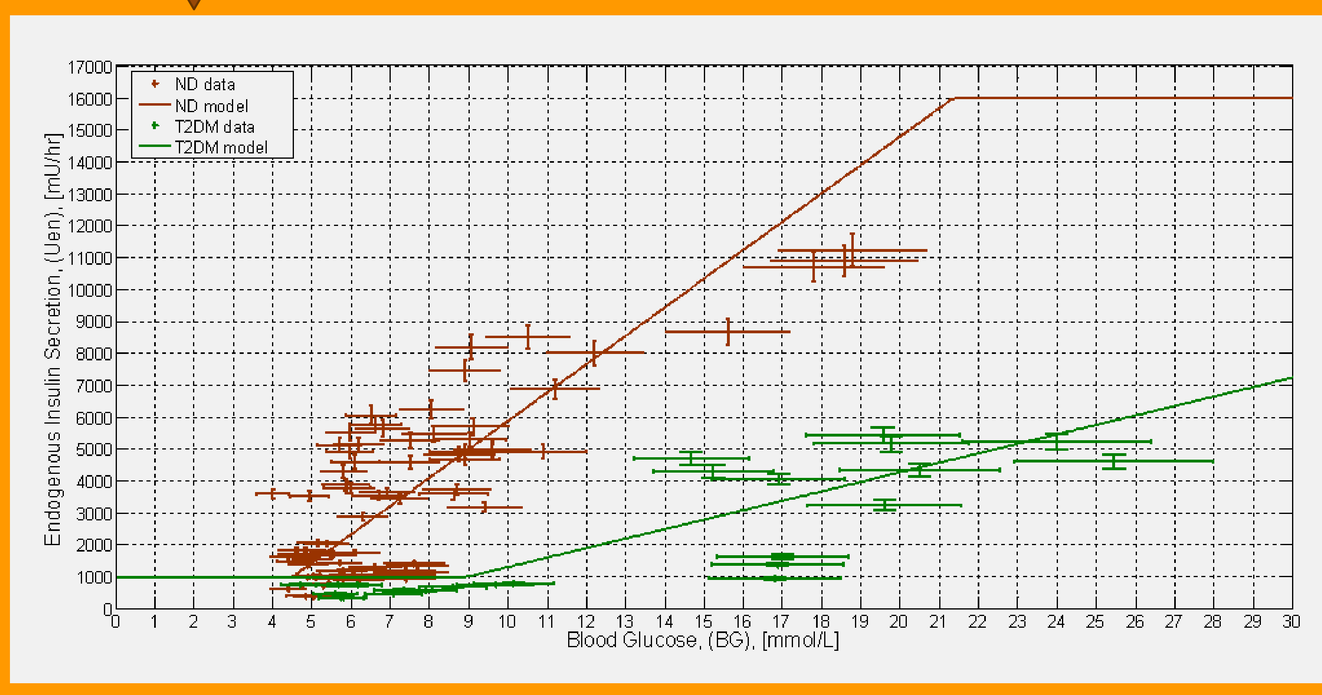
Results

- The best model for insulin secretion, in terms of both fit to data and simplicity is the 1-dimensional model based on blood glucose (BG) concentration alone.
- The clear separation between non-diabetic (ND) and T2DM patients suggests two separate models for insulin secretion (Uen):

ND: ***Uen = 893xBG – 2996*** constrained to [1000-16000] mU/hr

T2DM: ***Uen = 296xBG – 1644*** constrained to [1000-16000] mU/hr

- Model fits achieve coefficients of variation of $R^2 = 0.61$ and $R^2 = 0.69$ for ND and T2DM, respectively.
- The model slopes compare well with published data for healthy and diabetic individuals



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