Category 1 :**Endocrine disorders**
Category 2 :**Miscellaneous**

A311 - ***Validation of a virtual patient and virtual trials method for accurate prediction of TGC protocol performance***

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Introduction:

Effective tight glycemic control (TGC) can improve outcomes, but is difficult to achieve. In silico virtual patients and trials offer significant advantages in cost, time and safety for designing effective TGC protocols. However, no such method has been fully validated. This study tests 2 matched cohorts from the Glucontrol trial treated with different protocols. The goal is to validate the ability of in-silico virtual patient models and methods to accurately predict patient-specific and clinical trial glycemic outcomes.

Methods:

The analysis uses records for a 211 patient subset of the Glucontrol trial (Liege, Belgium). Glucontrol-A (N=142) targeted 4.4-6.1mmol/L and Glucontrol-B (N=69) targeted 7.8-10.0mmol/L. Cohorts were matched by APACHE II score, age and sex ($p>0.3$). The Glucontrol A cohort was slightly older ($p=0.04$). Virtual patients are created by fitting a clinically validated model to the data, yielding time varying insulin sensitivity profiles (SI(t)) that create in-silico virtual patients.

Model fit and intra-patient (forward) prediction are used to validate individual in-silico virtual patients. Self-validation (tests A protocol on Group A virtual patients; and B protocol on B virtual patients) and cross-validation (tests A protocol on Group B virtual patients; and B protocol on A virtual patients) assess ability to predict a clinical trial result.

Results:

Model fit errors were small (<0.25%) for Group A, Group B and the entire cohort (A+B), indicating model fitness. Median prediction errors were: 4.3, 2.8 and 3.5% for Group A, Group B and (A+B), indicating individual virtual patients were accurate representations of real patients. Self and cross validation results were within 1-10% of the clinical data for both Group A and Group B. Self validation indicated clinically insignificant model and compliance errors. Cross validation clearly showed that the virtual patients enabled by identified patient-specific SI(t) profiles can accurately predict the performance of TGC protocols different from those used to create the virtual patients.

Conclusions:

This study validates these virtual patients and in silico virtual trial methods, and clearly shows they can accurately simulate, in advance, the clinical results of a TGC protocol, enabling rapid in silico protocol design and optimization. It is the first rigorous validation of a virtual in-silico patient and virtual trials methodology.