Stress-induced hyperglycaemia commonly occurs during critical illness and has been associated with increased morbidity and mortality. The literature on glycaemic control and nutritional support does not provide consensus about optimal protocols for treatment. Concerning the control of blood glucose (BG), this thesis hypothesizes that mortality can be reduced by reducing BG and/or by reducing the frequency of hypoglycaemic events. It also hypothesizes that in clinical practice reduction of BG and hypoglycaemic events is best achieved by using model-based decision support systems. Concerning nutrition the thesis hypothesizes that nutrition should target the patient’s energy expenditure (EE), except for the first few days following the insult to the patient, where the caloric target should be below the patients EE. The thesis also hypothesizes that in clinical practice accurate estimation of EE cannot be done by predictive equations that use anthropometric data, but can be done by a novel method, CO₂-based calorimetry.

Evidence from the literature, including the four papers that are the basis of this thesis, will be used to examine each of these six hypotheses.

A two-dimensional regression based on data from clinical studies indicate that both reduction of BG (p=0.07) and reduction of severe hypoglycaemia (p=0.11) reduces mortality. A comparison of clinical studies support that model based decision support systems perform well. In particular the Glucosafe and STAR systems achieved substantial reductions of BG without provoking hypoglycaemic events. This provided the motivation for further improving the Glucosafe system (Paper I), which has two major components: a metabolic model and an advice module. To improve the Glucosafe model’s ability to predict BG, a model of pancreatic insulin release was constructed (Paper III). The pancreas model introduces a feedback loop in the Glucosafe model, which may produce instability. The model was found to be stable but also to produce damped oscillation after sudden changes in BG. A method based on virtual patients was developed to test the advice module. The virtual patients were used to evaluate different settings of the penalty functions that govern Glucosafe’s treatment advice (Paper II). This method makes it possible to assess the effects of changing the settings without a clinical trial.

Consensus regarding nutritional support for critically ill patients has not been reached in the literature. While there is support for not feeding the patient more than 100% of EE, as studies have shown this to have deleterious effects, some studies suggest targeting 100% of EE and some suggest targeting less than 100%. Regardless of the nutritional target, an accurate estimation of a patient’s EE is needed. The VCO₂-based calorimetry method estimates EE based on instantaneous VCO₂ measurements using a modification of the Weir formula that incorporates a respiratory quotient (RQ) value. The presented results (Paper IV) show that VCO₂-based calorimetry gives EE estimates significantly better than predictive equations.

In conclusion there seems to be support for, or no direct evidence to oppose, the 6 hypotheses stated.
To fulfill the requirements for the PhD degree, Mark Lillelund Rousing has submitted the thesis: Model-based Decision Support for Nutrition and Insulin Treatment of Hyperglycaemia in the ICU, to the Faculty Council of Medicine at Aalborg University. The Faculty Council has appointed the following adjudication committee to evaluate the thesis and the associated lecture:

Dr. James S. Krinsley  
Stamford Hospital  
Connecticut, USA

Associate Professor John Bagterp Jørgensen  
Department of Applied Mathematics and Computer Science  
Technical University of Denmark  
Denmark

Chairman:  
Associate Professor Claus Graff  
Department of Health Science and Technology  
Aalborg University  
Denmark

Moderator:  
Professor Steen Andreassen  
Department of Health Science and Technology  
Aalborg University  
Denmark

The PhD lecture is public and will take place on:

Friday 5 August 2016 at 13:00  
Aalborg University – Fredrik Bajers Vej 7E/3.209  
9220 Aalborg East

Program for PhD lecture on  
Friday 5 August 2016

by

Mark Lillelund Rousing

Model-based Decision Support for Nutrition and Insulin Treatment of Hyperglycaemia in the ICU

Chairman: Associate Professor Claus Graff  
Moderator: Professor Steen Andreassen

13.00 Opening by the Moderator
13.05 PhD lecture by Mark Lillelund Rousing
13.50 Break
14.00 Questions and comments from the Committee  
Questions and comments from the audience at the Moderator’s discretion
16.00 Conclusion of the session by the Moderator

After the session a reception will be arranged