MODEL BASED INSULIN SENSITIVITY AS A METABOLIC MARKER FOR SEPSIS IN THE ICU

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Introduction: Severe sepsis and septic shock occur frequently in the Intensive Care Unit (ICU) and are a leading cause of admission, mortality and cost. Around 11-12% of all NZ and US ICU admissions are due to the more extreme cases of severe sepsis. Currently, the diagnosis of sepsis presents many challenges in clinical settings. Sepsis treatment consists of antibiotic therapy with the use of fluid therapy and vasopressors. A positive blood culture for the specific sepsis type should precede the use of antibiotics and other therapies. Importantly, many of these therapies would be contra-indicated if sepsis wasn’t present. However, such blood culture results take 24-48 hours to process, by which time the disease may be advanced and more difficult to treat. Faster approximate diagnoses can be obtained in 4-8 hours using a variety of biomarkers, but with highly variable success. As a result, physicians often prescribe broad-based antibiotic and other therapies based on inconclusive data as a pre-emptive attack on the possibility of sepsis. A model-based insulin sensitivity was found to decrease with worsening condition and could thus be used to aid diagnosis.

Methods: Using a validated insulin-glucose regulatory mathematical model, the modelled insulin sensitivity ($S_I$) is evaluated against clinical sepsis diagnosis for 394 ICU patients totaling 26,453 patient hours who were on a glycemic control protocol. Patients with type I or type II diabetes were excluded. Ethics approval for this study was granted by the South Island Regional Ethics Committee. Receiver operating characteristic curve is calculated. A cutoff value for insulin sensitivity is determined, over which sepsis is unlikely to occur. Negative and positive predictor values are calculated. Correlation between model-based insulin sensitivity and sepsis score ($SS$) is calculated ($SS = 0-4$ for increasing severity). A simple sepsis indicator score ($SSI$) which can be calculated from a patient’s feed and insulin history at the bedside is developed to reflect model-based insulin sensitivity. This score is retrospectively tested against the 394 ICU patient’s sepsis diagnosis.

Results: Receiver operating characteristic cutoff values of $S_I = 8 \times 10^4$ L/mU/min and $SSI = 2.8 \times 10^4$ L/mU/min were determined for $SS \geq 3$. The model-based $S_I$ fell below this value in 15% of all patient hours. The $S_I$ test had a negative predictive value of 99.8%. The test sensitivity was 78% and specificity was 82%. Slightly lower sensitivity (68.8%) and specificity (81.7%), but equally good negative prediction (99.7%), were obtained for $SSI$.

Discussion: Model-based insulin sensitivity value provides an accurate negative predictive diagnostic for sepsis. The positive predictor value may be further improved by a more specific clinical symptom filter. Higher insulin sensitivity rules out sepsis for the majority of patient hours and can be determined noninvasively from glycemic control protocol data. Real-time indicator $SSI$ can be quickly calculated by the bedside and aid the decision on antibiotics usage. Clinical measurements such as blood pressure and heart rate derivatives may be further examined to enhance the accuracy of $SSI$. Low insulin sensitivity is not a sufficiently effective diagnostic, as it can equally mark the presence of sepsis or other conditions. Combining insulin sensitivity and other clinical measurements and medication history may lead to a better indicator for sepsis.

Conclusions: The use of model-based insulin sensitivity provides a non-invasive and quick indicator for the diagnostic of sepsis. Higher insulin sensitivity indicates the likelihood of sepsis, and thus prevents unnecessary antibiotic usage and the possibility of antibiotics resistance. Lower insulin sensitivity can be brought on by sepsis as well as a range of other conditions. Further study of clinical measurements and medication history may improve the accuracy of a sepsis indicator.