Computer assisted decision support in acutely ill patients. Application in glucose management and quantification of myocardial reperfusion

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Chapter 10

Summary and future perspective
Summary

This thesis describes the development and initial results of a set of computer assisted techniques in critically ill patients. Chapter 1 provides a general introduction to glucose control and myocardial perfusion.

Chapter 2 describes the development and evaluation of the “hyperglycemic index” (HGI), a quantitative measure of hyperglycemia in critically ill patients. This measure uses an area-under-the-curve approach that yields a value that incorporates all glucose measurements of a single patient. With the use of a predefined cut-off value, too low glucose values do not negate the impact of too high values, which is common in conventional measures of hyperglycemia. In a cohort of 1779 patients treated for at least 4 days at the intensive care unit, the HGI correlated better with 30-day mortality than other measures of hyperglycemia. Analysis of the quality of glucose control therefore should include all available measurements in a way that corrects for non-random sampling intervals by taking actual measurement times into account.

In chapter 3 we studied a cohort of over 6000 patients to identify differences in subgroups of critically ill patients with respect to glucose control. The correlation between HGI and mortality was significantly different in trauma patients compared with patients admitted for other reasons. The cause for this difference is unknown, but the markedly different baseline characteristics are likely to play a role. Due to the major difference in the pattern of glucose control, results from interventions on glucose control in general ICU patients may not be directly applicable to trauma patients.

In chapter 4, a before-after study was described. Two groups of patients admitted after coronary artery bypass grafting treated with different dexamethasone dosing schemes were compared. Starting at 4 hours after dexamethasone administration, glucose levels were higher in the high-dose group. Corrected for other factors, the difference in glucose level was maximal at 12 hours, amounting to 1.5 mmol/L. In the current era of tight glucose control, this is a clinically relevant difference. This finding underscores that administration of corticosteroids may be an important input parameter in a complex glucose control protocol.

Chapter 5 studies patients with acute ST-elevation myocardial infarction who received a high dose glucose-insulin-potassium infusion as part of the GIPS II trial. The study treatment induced marked hyperglycemia, resistant to high dosed insulin therapy in a significant proportion of patients. The induced refractory hyperglycemia was associated with larger myocardial infarction size as measured by enzyme release. The failure of GIK-trials in humans to reproduce the beneficial effects seen in animal experiments may partially be explained by the hyperglycemia that is induced by GIK. Future GIK schemes should aim to prevent hyperglycemia with a variable glucose
Summary and future perspective

infusion, as high doses of insulin cannot suppress hyperglycemia in some patients. The second part of chapter 5 reviews the future of glycometabolic interventions in patients with myocardial infarction.

In chapter 6, a computer program which assesses myocardial perfusion after primary coronary intervention for acute STEMI was developed. In a cohort of patients included in a randomized trial, the program successfully quantified perfusion on a large majority of angiograms. The quantified perfusion measure correlated well with outcome, as measured by ECG variables, myocardial enzyme release and death at 1 year. Future studies investigating interventions aimed at improving myocardial perfusion should preferably include a quantified endpoint such as provided by our program.

Chapter 7 describes the setup of “GRIP”, a computerized glucose control protocol. First, the Java GRIP program was developed in-house. This program queries nurses for clinical information of the patients to be treated. Data available from the central hospital information system was retrieved automatically. The program gave recommendations on insulin pump rates and glucose measurement intervals based on a simple control equation incorporating the current level of glycemia and the magnitude of change over the last 4 hours. The results in an initial cohort of 179 patients were promising. The rate of hypoglycemia was low with 4.9 (interquartile range 4.2-6.2) measurements per patient per day. The computer assisted protocol was well accepted by the nursing staff, who indicated that the protocol saves time otherwise spent on communicating with physicians.

Chapter 8 describes the results of a cohort of 2800 patients at three different intensive care units, for whom glucose control was managed by GRIP. The compliance with the protocol was high, and the low rate of hypoglycemia seen in the small cohort was confirmed. The glucose control process remained efficient with 5.9 (interquartile range 4.8 - 7.3) measurements per patient per day. This study confirmed that the positive results seen in the small study were generalizable to other units and held up in longer term routine practice.

In chapter 9 a before-after study was performed on the effect of a potassium control recommendation in GRIP. In addition to insulin pump rates and measurement intervals, this new version of GRIP (GRIP-II) generates recommendations on potassium administration. Compliance and acceptance of the protocol by the nursing staff were high. The median potassium levels with the GRIP protocol remained similar to those in the period before implementation of GRIP-II. The variability of potassium was reduced, and the incidences of both hypokalemia and hyperkalemia were significantly reduced.
Future perspective

In this thesis, computer assisted methods were shown to be able to improve research and clinical practice by standardized assessment of clinical data and relevant laboratory parameters. More complex analysis than taking a simple mean of measurements enabled more relevant information about glucose control to be distilled from measured glucose levels. With the further refinement of current treatment protocols, these analyses lead to quicker identification of promising algorithms.

A different step in glucose control where complex analysis is used may be continuous measurements. For the past decades, the technology to measure glucose continuously by a subcutaneous or intravenous sensor has been evolving slowly. Although these sensors are not yet feasible for use in routine practice due to low reliability and high costs, they can be useful in specific studies on short-term glucose changes. Continuous sensors can provide a higher time resolution than regular measurements, and therefore computer analysis of data will be mandatory especially for this type of measurement.

Further research on the analysis of glucose measurements may also reveal new tentative goals to aim for. Recently, glucose variability was found to correlate significantly better with mortality than the level of hyperglycemia. The control algorithm used by GRIP may be further refined in the future. The data gathered by GRIP can be used to build and validate new models for glucose control, which ultimately lead to even safer, more efficient glucose control. The addition of glucose intake recommendations will also be an important improvement to GRIP, especially to control the most insulin-resistant patients. Recently, promising results were reported with a protocol using a slide wheel guiding both insulin dose and glucose intake. More extensive analysis of data gained by GRIP can also identify further factors influencing glucose control, like the way trauma patients were identified as a specific subgroup of patients exhibiting patterns different from other patients. With the identification of these factors, the algorithm may be tuned to deliver more tailored recommendations. The gradual shift healthcare is making towards electronic management of patient data will facilitate the automatic identification of relevant factors, and lessen the need for nurses to input relevant information into GRIP manually.

Ultimately, when glucose, insulin and potassium are all controlled by GRIP, this will be the ideal situation to perform a new study on the effect of GIK in patients with acute myocardial infarction. A computer guided protocol can then titrate the three components of GIK independently. By administering this therapy under strict control algorithms, the potentially harmful side-effects in the form of derangements in glucose and potassium levels can be prevented and the true potential of GIK can
be assessed.

References
