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Specialist nurse's glycemic control in critically ill patients

A scoping review

Specialistsjuksköterskans glykemiska kontroll hos kritiskt sjuka patienter

En översiktsstudie

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ABSTRACT

Background: Stress induced hyperglycemia is a major global problem in the critical care setting and is strongly associated with adverse outcomes. Glycemic control is a complex task, and while there exist plenty of studies on the appropriate measures of dealing with it, the knowledge about factors influencing Stress induced hyperglycemia is still limited. **Aim:** The aim of this study was to illuminate nurses´ strategies to enhance health and well-being through glycemic control in critically ill patients. For this goal we apply Patrica Benner's 'from novice to expert to' concept. **Method:** A literature review with a qualitative approach was chosen to investigate the study's aim. 16 articles were included in this scoping review with a descriptive content analysis. **Result**: 6 themes appeared as different disorders that affect blood glucose regulation; Covid-19, Sepsis, Diabetes, Cardiology, Brain injuries and Treatment and other factors that affect blood glucose, which included the subthemes: medications, haemodialysis, nutrition and gender. **Conclusion:** Data suggests that a person-centered approach, considering different patient populations, should be applied to glycemic control in order to safeguard critically ill patients' health and safety.

SAMMANFATTNING

Bakgrund: Stressinducerad hyperglykemi är ett stort globalt problem i vården av kritiskt sjuka patienter och är starkt kopplat till ogynnsamma utfall. Glykemisk kontroll är en komplex uppgift. Trots att det existerar en mängd studier om det lämpligaste tillvägagångssättet att hantera det på, är kunskapen om faktorer som påverkar stressinducerad hyperglykemi fortfarande begränsad. **Syfte:** Syftet med den här studien var att belysa sjuksköterskors strategier för att förstärka hälsa och välbefinnande hos kritiskt sjuka patienter genom glykemisk kontroll. För detta ändamål applicerades Patricia Benners koncept 'från novis till expert'. **Metod:** En litteraturstudie med kvalitativ ansats valdes för att undersöka studiens syfte. 16 artiklar inkluderades i denna översiktsstudie med deskriptiv innehållsanalys. **Resultat:** 6 teman framkom som olika tillstånd som påverkar blodsockerreglering; Covid-19, Sepsis, Diabetes, Kardiologi, Hjärnskador samt Behandlingar och andra faktorer som påverkar blodsockret, vilket inkluderade subteman: medicinering, hemodialys, nutrition och kön. **Slutsats:** Data antyder att ett personcentrerat förhållningssätt och hänsyn till olika patientkategorier bör appliceras på glykemisk kontroll för att säkra kritiskt sjuka patienters hälsa och säkerhet.

INNEHÅLLSFÖRTECKNING

ABSTRACT 1

SAMMANFATTNING 2

1. INTRODUCTION 5

2. BACKGROUND 5

2.1 Health, well-being and person-centered care 6

2.2 Intraoperative and postoperative high blood glucose 7

2.3 Stress Response 8

2.4 Stress response following surgery 9

2.5 Novice to expert: Excellence and Power in Clinical Nursing Practice 9

2.6 Not too much, not too little 10

2.7 The specialist nurse's intervention 12

3. RATIONALE 12

4. AIM 13

5. METHOD 13

5.1 Design 14

5.2 Sample 14

5.3 Data collection 15

5.4 Data analysis 16

5.5 Ethical considerations 17

6. RESULTS 17

6.1 Covid-19 (SARS-CoV-2) 17

6.2 Sepsis 18

6.3 Diabetes Mellitus (DM) 19

6.4 Cardiology 20

6.5 Brain injury 20

6.6 Treatments and other factors that affect blood glucose 21

6.6.1 Medications 21

6.6.2 Haemodialysis 22

6.6.3 Nutrition 22

6.6.4 Gender 23

7. DISCUSSION 23

7.1 Discussion of methods 24
7.1.1 Design of the study 24
7.1.2 Sample 24
7.1.3 Data collection 25
7.1.4 Data analysis 25
7.2 Discussion of results 26
7.2.1 COVID-19 26
7.2.2 Sepsis 27
7.2.3 Diabetes Mellitus 28
7.2.4 Cardiology 30
7.2.5 Brain injury 31
7.2.6 Treatments and other factors that affect blood glucose 33
7.2.6.1 Medications 33
7.2.6.2 Haemodialysis 34
7.2.6.3 Nutrition 35
7.2.6.4 Gender 36
8. CONCLUSION 37
8.1 Clinical implications 37
8.2 Future research 37
9. REFERENCES 39
APPENDIX 51
Appendix 1 – Search Matrix 51
Appendix 2 – Article Matrix 52

1. INTRODUCTION

Hyperglycemia relates to an increased risk for negative outcomes (Duggan & Chen, 2019) including mortality, especially in non-diabetic patients (Jones, et al., 2016). The core competencies of a registered specialist nurse in Sweden includes the provision of evidence-based and safe care, the constant improvement of knowledge and quality development, as well as a person-centered care (PCC) (Svensk sjuksköterskeförening, 2020). Ekman, et al. (2011) means PCC shifts focus from the disease to the person and his/her preferences, experience, beliefs and feelings. We would like to shed light on glycemic control, especially in managing Stress Induced Hyperglycemia (SIH), based on current evidence, to facilitate that aspect of the specialist nurse's clinical practice. Doing so would promote health and increase patient safety, as it otherwise would result in adverse outcomes. Health promotion is a fundamental part of nursing practise. According to several studies and our experiences as nurses at two different public Swedish hospitals, glycemic control is a complex task and goes beyond taking blood gas samples and administration of insulin. Therefore, a coherent strategy for a good and safe glycemic control is needed. Such a more advanced task goes hand in hand with the need of a person-centered approach as well as personal skills of the specialist nurse towards patient safety and quality of care.

2. BACKGROUND

Quality of care is considered a fundamental global social health problem and puts patient safety at risk (Samokhvalov, Farah & Makhoul, 2012). Over several decades many studies tried to elucidate the optimal blood glucose targets in critically ill patients, as well as the best methods to monitor, reach and/or control blood glucose targets. Especially the results regarding concrete glucose targets are not always consistent and sometimes even contradictory. Which in turn jeopardizes the patient's safety.

Even though glycemic control is a common and important core task for intensive care unit (ICU) or operating room nurses, there are few studies assessing their role in this regard. Several factors, often in combination, affect how the patient will react to continuous intravenous insulin therapy (CIIT) and glycemic control. Thus, glycemic control of critically ill patients is a

complex task (van Hooijdonk, Mesotten, Krinsley, Schultz, 2016). Requiring good knowledge about evidence and a person-centered care. An underestimation of this task (both from a physician's and/or a nurse's perspective) puts patient safety at risk and could negatively affect quality of care.

Glycemic control aims to avoid or monitor hyperglycemia, hypoglycemia and glycemic variability, as several studies associate them to an increased morbidity and mortality in critically ill patients (Murphy, Saliba, MacDermott, Soe & Dungan, 2020; van Hooijdonk et al., 2016). In the perioperative setting a variating but relevant number of patients may experience problems with blood glucose regulation. This is regardless of a diagnosis of diabetes mellitus (DM) or pre- diabetes (Brutsaert, Carey & Zonszein, 2014). Its treatment with CIIT can be a double-edged sword, being one of the possible reasons for developing hypoglycemia (Samokhvalov et al. 2012). As hypoglycemia is linked with poor outcomes and considered a risk factor for negative vascular events and mortality (Yeh, et al., 2016). It becomes a challenge for the specialist nurses to facilitate the wellbeing in the patient with glycemic variability. In order to facilitate that challenge, our intention is to use the latest research on the subject and apply them to elucidate possible nurses' strategies in those studied patients' populations.

2.1 Health, well-being and person-centered care

World Health Organization (2020) means that the term "health" is not simply an absence of a disease but a state of total physical, mental and social well-being, and is a fundamental right of all human beings. This statement makes the individual aspect of glycemic control pivotal and as described above, PCC is vital to the patient with glycemic variability. Pelzang (2010) describes PCC as treating patients as individuals, considering their points of view, and treating them with respect. PCC entails, according to Ekman, et al. (2011), putting the person before the disease they have, making the impact the disease has on their life, center of the care. This captures the suffering as narrated by the patient, as opposed to medical records that center the disease with its diagnosis and treatments (Ekman, et al., 2011). Caring for the patient with compassion and strengthening their integrity are important components of PCC, along with including the patient in discussions about their health (Jardien-Baboo, van Rooyen, Ricks, Jordan & Ham-Baloyi, 2020). According to Swedish Healthcare Laws, care should be planned and implemented in consultation with the patient, as far as possible (Patientlag, SFS 2014:821,

5 kap, 1 §). In addition to this, studies on PCC indicate better outcomes and a reduction in health care costs (Pelzang, 2010)

There are several aspects of well-being, two of them being described by Sonnentag (2015) as a subjective feeling-good experience and having a meaningful life. Sonnentag further describes how well-being might fluctuate within different time intervals, both short intervals within a day, but also longer ones for example from day-to-day or even week-to-week. Well-being is described by Crisp (2017) in the Stanford Encyclopedia of Philosophy as what is considered to be ”good” for a person, and the term ”health” might be a part in the person’s well-being. PCC, in the way described above, may be difficult in the care of critically ill patients who cannot express what health means to them, but we must assume that treating the critical illness and SIH will contribute to restoring their health, because of the adverse outcome that could otherwise arise.

The first to notice a change in the patients’ status is the nurse, because of the constant interaction between nurse and patient. Detecting physiological changes is therefore, between other things, where nurses play a fundamental role in care (Bleakley & Cole, 2020). According to Pinto Martins Barreto, Tonini & Gerbassi Costa Aguilar (2013) some important tasks for a nurse in a critical care setting is to identify the patient’s clinical state and the moment to intervene. In order to do that, it is required that the nurse has decision-making skills and broad theoretical and practical knowledge, to be able to make the correct decisions.

2.2 Intraoperative and postoperative high blood glucose

Critically ill patients are complex, sensitive and need medical and surgical care, intensive care and close monitoring to be able to survive (Abdulai, 2015).

In healthy individuals in normal situations, the balance between the amount of glucose that the liver produces, and the amount used in tissues is carefully regulated by various hormones and mechanisms. This causes the blood glucose concentration to be kept normal (normoglycemia/euglycemia). But the stress to which the body is subjected during surgery and anesthesia changes this balance and hyperglycemia can occur (high blood glucose) (Duggan, Carlson & Umpierrez, 2017; Sharabi, Tavares, Rines & Puigserver, 2015). It is then easy to understand that when the patient has a disease or a condition that carries an actual or potential high risk of dying, the patient is critically ill (Medical Dictionary, 2020).

Stress induced hyperglycemia (SIH) is a temporary increase in blood glucose values, caused by insulin resistance initiated because of a stressor in the body (Dungan, Braithwaite & Preiser, 2009). The prevalence of SIH varies a great deal from around 20% in hospitalised patients (Zelihic et al., 2015), up to as much as 50% (Plummer et al., 2014) or even 75% in critically ill patients (Shi et al., 2016). These varying numbers make drawing conclusions about the prevalence of SIH difficult, which is also described by McCowen, Malhotra and Bistrian (2001). Accumulating scientific evidence connects SIH to negative outcomes; a systematic scoping review (Olariu, Pooley, Danel, Miret & Preiser, 2018), showed that several studies consistently linked high blood glucose values with increased risk of mortality, infections and longer ICU/hospital stay. Shi, et al. (2016) explains that SIH can also lead to severe complications such as hypoglycemia (low blood glucose) and hyperosmolar coma events.

After a long time going in different directions there is, according to the latest published review, an international expert consensus between ICU caregivers to treat blood glucose concentration > 10 mmol/L. in all patients receiving intensive care. The goal is to achieve and maintain values between 7.77 and 10 mmol/L in order to have a margin to ward off hypoglycemia and treat hyperglycemia, but the optimal targets are not established yet (Eerdekens, Rex & Mesotten, 2020). There are different methods and ways to control blood glucose levels with different accuracy (Seley, Diaz & Greene, 2016). It is recommended using arterial blood samples to avoid inaccurate results because of peripheral edema and emphasize the importance of controlling blood glucose measuring devices periodically (Seley, Diaz & Greene, 2016). Further on, they highlight the importance of protocols to treat hypo- and hyperglycemia and refer to them as important standards of practice (Eerdekens et al., 2020).

2.3 Stress Response

According to Russell and Lightman (2019), when the body is affected by a stressor, it responds by activating several coordinated and dynamic processes to reinstate homeostasis that is needed for maintaining life and at the end, reach evolutionary success for humans. A stressor in this situation is a stimulus that threatens to disturb the homeostatic balance. When the body is, or feels threatened, an additional homeostatic mechanism activates: the human stress response. This mechanism involves neural and hormonal processes that increase cognitive, cardiovascular, immunological and metabolic function with survival as goal. The human stress response is coordinated and synchronized for a system, the hypothalamic–pituitary–adrenal

(HPA) axis. This system, as well as cortisol metabolism are regulating mechanisms that play an important role in the presence of short-term and longer-term stress (Russell & Lightman, 2019).

2.4 Stress response following surgery

As part of the stress response, a cascade of several biological mechanisms, called the inflammatory reaction, happens when harmful factors (virus, tissue damage, etc.) affects the body (Löwbeer, Hammarsten, Rönnelid, Ridefelt & Theodorsson, 2018). High release of inflammatory cytokines occurs (Duggan, et al., 2017) and together with tumor necrosis factor induce most of the manifestations of the inflammatory reaction. This reaction causes several metabolic effects that are proportionately related to the intensity and size of the inflammation (Löwbeer et al., 2018).

When the body is exposed to for instance surgery and trauma, the stress response is activated and metabolic and hormonal counter-regulating processes take place. The body secretes catecholamines, glucagon, cortisol and growth hormone (Duggan, et al., 2017; Desborough, 2000). Cortisol secretion promotes liver glucose production (gluconeogenesis), protein catabolism and glycogenolysis. Through an oxidative mechanism, high blood glucose concentrations circulating in the blood, result and contribute to increased blood concentration of cytokines (Esposito, et al., 2002). Catecholamines increase the secretion of glucagon, which in turn causes glucose to leave the cells and the beta cells found in the islets of Langerhans in the pancreas to not secrete insulin. The secretion of catecholamines increases lipogenesis which leads to an increase in blood concentration of "free fatty acid" (Duggan, et al., 2017) and leads to inhibition of insulin-stimulated glucose uptake into skeletal muscle cells (Roden, et al., 1996). A consequence of this is a relative insulin resistance, which has shown to be individual and lasts at least five days, is greater on the first day after surgery and usually disappears twenty days after surgery (Thorell, Efendic, Gutniak, Häggmark & Ljungqvist, 1994). A specialist nurse needs to know such things to enhance the quality of care and safeguard her patient.

2.5 Novice to expert: Excellence and Power in Clinical Nursing Practice

Novice to expert is a theory formulated for Patricia Benner. She states the base knowledge of nursing discipline should be created through the time, by its practice (know-how) and through

scientific investigations (know-that) and observation to develop clinical expertise, also described by Benner (1993) as connoisseurship. Benner describes connoisseurship as a kind of "knowing" that gives nurses the possibility to improve their skill base.

Benner describes a situation-based model consisting of five levels of skill acquisition from novice to expert. The levels are novice, advanced beginner, competent, proficient, and expert. Further on, Brykczynski (2010) explains that in nursing, knowledge develops with practice and develops through time. Changes in four levels of knowledge and performance allows for the movement from novice to expert over time and through extending practical clinical knowledge with theoretical knowledge (Brykczynski, 2010). Benner further explains nursing as "reasonable behaviour that responds to the demands of a given situation". Implementing skilled nursing interventions together with clinical judgments skills in clinical situations is defined for her as skilled practice. Such skilled practice for instance needed to plan a good and safe glycemic control strategy that meets the unique patients´ needs.

In this study, the idea is that by gaining knowledge about what evidence recommends in glycemic regulation, the specialist nurse can increase the "know-that", to combine it with "know-how" in the way towards development to expertise and development of connoisseurship. This increase in nursing skills could result in an increase in quality care. In order to achieve good quality of care, a combination of evidence based, and safe care should be given together with PCC. This could reflect in an increased patient safety.

2.6 Not too much, not too little

On one hand, gluconeogenesis, glycogenolysis and lipolysis are promoted and increase the blood glucose level. And in another, insulin release and insulin stimulated glucose uptake are inhibited, leading to relative insulin resistance, which results in hyperglycemia (Duggan, et al., 2017) since there is much glucose in the blood that the body cannot use. Continuous intravenous insulin infusion is used in intensive care units to treat hyperglycemia by reducing the level of glucose in blood and has shown to be the best method of doing so (Pérez, Ramos & Carreras, 2020). Continuous insulin therapy helps to improve glycemic control when the patient does not present hypoglycemia (Biolo et al., 2018) but is also related to a significant increase in hypoglycemic events and could not relate to a significant reduction in mortality in critically ill patients (Chen, 2010). Hypoglycemia could result in harmful consequences for the patient

(Koraćević et al., 2020) and it is important that the nurse acknowledges this fact when caring for these patients.

There are different methods with different target values for treating hyperglycemia. Some studies advocate Intensive Glycemic Control (81-108 mg/dl. [4.5-6.0 mmol/L]), others recommend conventional glucose control (180 mg/dl. [10.0 mmol/L]), research has disagreed on which method is best. (According to Diabetes.co.uk [2019] conversion from mmol/L to mg/dl is done by multiplying the value with 18. Any blood glucose values in this paper will be reported in mmol/L). It is important to consider that some studies show that sometimes treating hyperglycemia can lead to other life-threatening states, such as hypoglycemia, putting the patient's safety at risk (Chittineni et al., 2019).

Research has been contradictory in the last decades. Hyperglycemia (if not over 12.5 mmol/L) was considered protective until a large trial called the Leuven clinical trial (van den Berghe, et. Al., 2001). This study showed that hyperglycemia had negative effects and recommended tight glycemic control to decrease mortality, although these results could not be proven again. An international and larger randomized controlled trial, The Normoglycemia in Intensive Care Evaluation-Survival Using Glucose Algorithm Regulation (NICE-SUGAR) study, showed that tight glycemic control did not decrease mortality but, on the contrary, significantly increased the cases of hypoglycemia. They reported severe hypoglycemia in 6.8% of the patients in the intensive glucose control in contrast with 0.5% in the conventional glucose control group. The NICE-SUGAR study investigators found a considerable decrease in 90 days mortality and the cases of hypoglycemia by adopting a conventional glucose control (10 mmol/L or less) compared to intensive glucose control (4.5-6 mmol/L) (Finfer et al., 2009). Furthermore, in another study the authors confirmed that intensive glucose control causes moderate and severe hypoglycemia and stated that both are associated with a higher risk of death (Finfer, 2012). However, this new recommendation did not fast replace the harmful old one, especially in the United States (Niven, Rubenfeld, Kramer, & Stelfox, 2015). In the same line, a systematic review found no decrease in mortality by tight glycemic control in critically ill patients but fivefold more hypoglycemia than in a mild or very mild control (Yamada, Shojima, Noma, Yamauchi, & Kadowaki, 2016). Late studies recommended starting treatment for hyperglycemia with intravenous insulin therapy when blood glucose concentration is higher than 10 mmol/L trying to keep it between 7.8-10 mmol/L (Clodi, Resl, Abrahamian, Föger &

Weitgasser, 2019). However, Murphy et al. (2020) found that no glucose range target suits all critically ill patients, suggesting individualisation is appropriate.

2.7 The specialist nurse's intervention

To maintain and facilitate the well-being in the critically ill patient, blood glucose control is vital, however, it is a complex process that can be influenced by various factors (Roosmarijn, et al., 2016). There are various methods for monitoring B-glucose in critically ill patients, according to Seley, Diaz & Greene (2016). Intensive care nurses usually check blood glucose by taking a blood gas from an artery or vein and analysing it in a blood gas device which also gives the nurse other important blood values, such as pH and electrolytes. This is an important process that allows the specialist nurse to adjust the amount of continuous intravenous insulin infusion that the patient needs, based on the results of the blood gas analysis in order to reach the desired target for blood glucose concentration (Seley, Diaz & Greene, 2016).

With Benner's theory, as defined above, in mind; learning these varying factors, analysing the blood gases and enforcing appropriate intervention, the nurse may improve their skill base. With the connoisseurship that this knowledge would lead to, they tend to the patient and their well-being, as well as increase in patient safety by the act of person-centered care.

3. RATIONALE

Stress induced hyperglycemia often occurs after a major surgery and has a big impact on patient health. Its treatment, however, is one of the main reasons for hypoglycemia (Koraćević et al., 2020; Chittineni et al, 2019). Perioperative hyperglycemia, hypoglycemia and glycemic variability in critically ill patients, have been linked to adverse consequences, higher morbidity, and mortality (Van den Berghe et al. 2009; Seley et al., 2016; Clodi et al., 2019), as well as an increased risk of developing type 2 diabetes in the future (Plummer et al., 2016).

Thus, the regulation of B-Glucose with intensive insulin therapy is challenging and requires nurses and physicians that are up to date with current research in this field (Seley et al., 2016). There exist plenty of studies regarding the best method of controlling blood glucose in critically ill patients (be it nurse-directed, protocol-based or with the use of technical equipment).

However, the method of blood glucose management varies between hospitals and is normally nothing nurses can individually decide on.

Despite the multitude of method-focus research, the knowledge about the impact of other factors on blood glucose control, such as underlying medical conditions, nutrition, medications, or gender, is still limited. Ndebu and Jones (2018) found in a study that increased mortality related to hypoglycemia was a widely known fact among the nursing staff, however only 25% of nurses on critical care wards recognised the symptoms of hypoglycemia.

Respective guidelines at the care units, as far as they exist, are often unknown or hard to access. Accordingly, this study focuses on summarizing and systemizing such factors and their effect on blood glucose management. This will allow specialist nurses to minimize the risk for negative outcomes that potentially could be controlled with a person-centered care based on respective expertise. Thus, it will help specialist nurses achieve the necessary connoisseurship to give safe and quality care for critically ill patients.

4. AIM

The aim of this study was to illuminate nurses' strategies to enhance health and well-being through glycemic control in critically ill patients.

In a first step we summarize and categorize international research results regarding glycemic control, especially in managing stress induced hyperglycemia (SIH). In a second step we apply these results on the clinical practice of the specialist nurse in Sweden in order to elucidate strategies enhancing health and well-being of patients through glycemic control.

5. METHOD

A literature review with a qualitative approach was chosen to investigate the study's aim. The benefits of a literature review are described by Knopf (2006) as yielding a general overview of research that one is not familiar with, revealing already successfully done research (to

prevent wasting time ”reinventing the wheel”) and to determine flaws in, or lack of, research already existing.

5.1 Design

Development of knowledge can be based on literature reviews (Snyder, 2019). Therefore, a scoping review was chosen in this study. According to Sucharew and Macaluso (2019) scoping reviews are useful when searching for answers to broad research questions and the purpose is to provide a summary of available research on a topic. Even though Polit and Beck (2017) describe systematic literature reviews to have the highest value of evidence in nursing, because careful synthesis of data from multiple studies forms the most reliable results, it would have been difficult to conduct since this study was investigating several aspects of the research area. If a more limited approach had been chosen, for example if the authors of this study had decided to focus on just a single influencing factor, a systematic approach would have been more suitable. Snyder (2019) means that a systematic approach to investigate a large research field is unsuitable, or even impossible. Therefore, the authors of this study decided a scoping review was more suitable. Polit and Beck also describe how literature reviews may be used to investigate whether there are gaps in knowledge in a certain area of research, and therefore contribute to existing evidence by noting what might be missing and suggest how to fill those gaps in evidence.

5.2 Sample

This study includes articles published in the Pubmed and CINAHL (Cumulative Index to Nursing and Allied Health Literature) databases. The articles are no older than 5 years, peer reviewed and available in full-text for free through the Södertörn university library alternatively through Stockholm Region library. As regards to the content of the studies, only studies on adult, not pregnant patients were reviewed. This limitation was chosen because of the difference in physiology in children and pregnant individuals. As the age limit differs between different studies the authors of this study let the authors of the original studies determine that age limit. After careful consideration, the authors of this study decided to only include studies where different circumstances that influence development and treatment of SIH were presented and described, as the methodology of glycemic control is decided by each hospital on their own.

Both qualitative and quantitative approaches were considered. The chosen articles were exclusively written in English.

Exclusion criteria includes: low quality, lack of ethical approval, studies where a commercial interest is seen, review articles, and literature studies. Further studies with a very small patient sample (20 or fewer participants) were excluded, along with studies where the aim was to validate a protocol or instrument.

5.3 Data collection

When collecting data for this study, the previously mentioned databases (Pubmed and CINAHL) were used to conduct several searches with carefully selected keywords according to the aim of this study. The resulting articles were initially included or excluded based on the title and abstract matching the aim of this study. After this initial exclusion process the entire article was read by both authors to determine whether the studies could give important information related to the aim of the study. This data collection process for literature reviews is described both by Polit and Beck (2017) and Snyder (2019).

Searches in CINAHL were conducted using Boolean phrases involving Nurs*, glucose control, critica* ill, critical care, stress hyperglycemia, stress induced hyperglycemia and SIH. In PubMed database, searches were conducted using the previously mentioned terms, but also involving other terms such as glycemic, glycaemic control, blood glucose, stress induced hyperglycemia, critical illness and MeSH Terms such as Nursing, blood glucose and critical care. The selected keywords are presented in tables (Appendix 1 - Search Matrix) together with the number of articles matching each search and how many of them were selected.

The searching of data from these databases have resulted in 7 articles from PubMed, 3 articles from CINAHL and 4 articles that were found in both databases. Meaning that from 480 hits, 14 articles were chosen. Beyond these database searches 2 articles have also been found through manual searches. Resulting all together in the 16 carefully chosen articles representing recent research and that this literature review is based on.

The searches resulting in any selected articles are separately presented as an appendix. Also, an appendix is attached presenting all the articles selected, along with the aim, methodology and conclusion of the study.

The quality of the research articles was rated using the questions from a form suggested by Polit and Beck (2017). The forms were rigorous, containing many yes/no questions which were copied and subsequently answered for each of the studies. One article was excluded in this process as the majority of the results were not statistically significant and the authors decided these results were not reliable enough to include in this review.

5.4 Data analysis

Data was analysed through a descriptive content analysis. Data from the studies were extracted and paired using the similarity principle using the selective approach. The selective approach is described by Polit and Beck (2017) as researchers pulling out or highlighting statements, they consider answering the research question at hand. Descriptive content analysis interprets findings from previous studies in order to prevail tendencies in that specific field (Dinçer, 2018).

Polit and Beck further describe how qualitative and quantitative data can be used to form a mixed method study by using what they call an integrated design, which can be used when studies are grouped up by findings considered to answer the same research questions, rather than grouped by method. This can be done by quantitizing qualitative findings or qualitizing quantitative findings, meaning using qualitative data quantitatively or vice versa.

Data analysis in this study is based on quantitative data using qualitative descriptive content analysis. The first step in the analysis process was therefore to qualitize the data from these quantitative studies. This was done by extracting the qualitative properties of the data, in this case the descriptions of the interaction between the diseases and factors on BG. Subsequently, data was reduced by identifying keywords, followed by construction of themes and subthemes using the similarity principle, as described by Polit and Beck. In this case, keywords consisted mainly of different factors and variables that influence blood glucose levels or the management of such. After identifying these keywords, they were bunched together and presented based on similarity by influencing factor.

5.5 Ethical considerations

There are various codes of ethics that have been developed. There are both international ethical standards, codes developed by each research discipline of their own and governmental, national guidelines. The codes of ethics are in place to protect human rights. Generally, in studies where there is an intervention the researchers make sure that the benefit outweighs the risks. This is called beneficence and ensures researchers minimize harm and maximize benefits. Further, informed consent is obtained from participants (or other legal representatives when the participant themselves cannot express consent) in original studies for example where there is an intervention. Although in cases where data is obtained anonymously, for example from medical records, the information is de-identified to assure the participants of anonymity. When anonymity is not possible, instead confidentiality is promised. There are different ways of accomplishing this, for example by letting the researchers that do have access to personal information sign a confidentiality pledge. Lastly, fair treatment of the people is promised, whether or not they decide to participate in the study (Polit & Beck, 2017).

Ethical aspects while conducting a literature review consist of making sure the authors of the original studies have ethical aspects described in the article, as well as described ethical approval. The authors of this review made sure the original studies included both ethical considerations and described obtained ethical approval from an institutional review board.

6. RESULTS

The data analysis resulted in 6 themes, one of them including 4 subthemes. The themes appeared as different disorders that affect blood glucose regulation; Covid-19, Sepsis, Diabetes, Cardiology, Brain injuries and Treatment and other factors that affect blood glucose, which includes the subthemes: Medications, Haemodialysis, Nutrition and Gender.

6.1 Covid-19 (SARS-CoV-2)

There appears to be a cause-effect relationship between SARS-CoV-2 and hyperglycemia. Meaning a larger number of patients with COVID-19 (without a prior diagnosis of DM), had a

higher degree of hyperglycemia than expected in a critically ill population developing SIH. This relationship was seen by Ilias et al. (2020) who also states that this could lead to complications in the form of other infections in this study population. Making it an important reason to treat hyperglycemia in this group of patients, according to the authors. Further on, out of the 11 patients who had died during the study period, seven (meaning more than half) of them had hyperglycemia. Being considered another example of why, besides other things, hyperglycemia in this group of patients should not be overlooked.

6.2 Sepsis

Hyperglycemia, hypoglycemia and glucose deviation are all linked to worse outcomes in the intensive care of septic patients. This is important to consider since the prevalence of stress-induced hyperglycemia in patients suffering from septic shock is high, according to Treskes, Koekkoek and van Zanten (2019). Regarding glucose deviation, meaning both hyper- and hypoglycemia, Wernly et al. (2019) showed that it increases the intra-ICU mortality. Further on, a study by Chan et al. (2016) showed that hypoglycemia (less than 6.6 mmol/l) in non-diabetic septic patients, measured at some point during glycemic control in the first 72 hours from admission, increased 14-day mortality, making hypoglycemia an independent risk factor. To prevent glycemic variability, hypoglycemia and hyperglycemia, Treskes et al. (2019) recommends initial restriction, if possible, of nutrition during the first critical 24 hours alternatively frequent glucose measurements as well as a higher blood glucose targets, which is also recommended by Chan et al. (2016).

The study by Treskes et al. (2019) showed that septic patients are more resistant to insulin therapy during the first 36 hours after admission to the ICU. The insulin resistance increased linearly during this time and peaked at that point, meaning the largest dose of exogenous insulin was required at 36 hours from admission. After 36 hours insulin resistance starts to decrease, therefore less compensation is required, allowing a lower dose of exogenous insulin administration (Treskes et al., 2019). The decline in IR combined with glucose variability could potentially result in insulin overdose and therefore causing hypoglycemia. A study by Chan et al. (2016) showed that hypoglycemia (less than 6.6 mmol/l) in non-diabetic septic patients, measured at some point during glycemic control in the first 72 hours from admission, increased

14-day mortality, making hypoglycemia an independent risk factor. To prevent glycemic variability, hypoglycemia and hyperglycemia, Treskes et al. (2019) recommends initial restriction, if possible, of nutrition during the first critical 24 hours alternatively frequent glucose measurements as well as a higher blood glucose targets, which is also recommended by Chan et al. (2016).

6.3 Diabetes Mellitus (DM)

DM is the largest contributing risk factor for suboptimal blood glucose control in critically ill patients, according to Becker et al. (2020). However, diabetic patients seem to tolerate hyperglycemia better than non-diabetic patients (Wernly et al., 2019; Johnston, et al., 2017), but are just as sensitive to hypoglycemia (Wernly, et al., 2019; Chan, et al., 2021). For example Wernly et al. (2019), investigated how different glycemic events affected patients with type 2 diabetes mellitus (T2DM) and without DM hospitalized with acute heart failure, pulmonary embolism, status post cardiopulmonary resuscitation (CPR) and sepsis. Patients with at least one single glucose deviation, had an increased risk for adverse outcomes, such as higher ICU and long-term mortality. According to the authors, patients with T2DM seem to be more sensitive to hypoglycemia than hyperglycemia but often develop severe hyperglycemia. In that group of patients, one episode of hypoglycemia, but no hyperglycemia, was also associated with increased ICU and long-term mortality. In that line, tolerating higher target values, even as high as 11.1 mmol/l might be acceptable (Wernly et al., 2019).

Further on Chan, et al. (2021) found, after a subgroup analysis, that blood glucose values equal or less than 6.66 mmol/L during the first 72 hours after admission, represented an independent risk factor for 14-day mortality in non-diabetic patients with sepsis, but not for patients with sepsis and DM. This leads to the conclusion that hyperglycemia should be treated more aggressively in patients without DM than those with T2DM. Hypoglycemia should, by all means possible, be avoided in both groups. Considering this, they recommend different approaches on blood glucose targets depending on underlying concomitant diseases (Wernly et al., 2019).

6.4 Cardiology

Meng et al. (2021), Kojima et al. (2020), Qin et al. (2019) and Gao et al. (2020) all found that hyperglycemia was associated with adverse outcome in patients with acute myocardial infarction (AMI). For instance, Qin et al. (2019) found that high fasting blood glucose was a risk factor for the MI to be classified as more severe and Meng et al. (2021) demonstrate an association between SHR and worse recovery of the ejection fraction (EF) in patients with ST-elevation myocardial infarction (STEMI). SHR was found to have a significant correlation with negative remodelling of the left ventricle and is considered to be the dominating cause of negative outcome. Patients that had STEMI and higher SHR had, according to Gao et al. (2020), a higher mortality. Along these same lines, Kojima et al. (2020) found that SIH impacted STEMI patients with and without DM differently. They found that mainly patients without DM who had high SHR were more likely to have worse long-term prognosis. A study by Wernly et al. (2019) also showed that intra ICU-mortality increased with glucose variability in, among others, patients with AMI, as well as patients being treated post CPR.

Johnston et al. (2017) took another focus and showed that hypoglycemic events are associated with both higher mortality and morbidity in cardiac surgery patients. The authors remarked that a combination of both hypo- and hyperglycemia constitutes a significant increase in risk. However, Johnston et al. (2017) do not demonstrate a causal relationship between the negative effects and hypoglycemia but that there is an association, meaning they could not determine whether the negative effects are the cause or a result of hypoglycemia. Leading to their conclusion that hypoglycemia should, if possible, be avoided and one might even allow mild hyperglycemia, but the authors emphasise that they cannot recommend a specific blood glucose target (Johnston et al., 2017). However, Qin et al. (2019) urges prompt intervention to lower blood glucose levels and Gao et al. (2020) advocates the use of calculating SHR to be able to adapt the treatment of hyperglycemia in patients with STEMI.

6.5 Brain injury

Hyperglycemia in patients with brain injuries is related to worse outcomes. For example, Khajavikhan, Vasigh, Kokhazade and Khani (2016) explain that hyperglycemia might serve as a predictive factor for several negative events compared to patients who did not have hyperglycemia. För instance, higher mortality, longer ICU and hospital stay, higher injury

severity score and prevalence of ventilator acquired pneumonia and acute respiratory distress syndrome. Along these same lines Ye et al. (2020) found a significant relationship between SHR and the occurrence of a type of secondary brain injury in patients suffering from intracerebral haemorrhage. This relationship, however, was not seen in hyperglycemic diabetic patients.

Another example is shown in a study by Oh, Lee, Shin and Seo (2019) who studied patients with brain injuries and compared one group with good neurological outcome and one with bad outcome. The blood glucose levels for both groups peaked during the first 72 hours before decreasing. In the bad recovery group, however, the blood glucose levels arose again after 6 days and remained high but with more variability, while in the good recovery group it continued to decrease linearly to normal levels. They also found factors that influence the development of SIH (in falling order); steroid use, total daily caloric intake, gender, APACHE II score (Acute Physiologic Assessment and Chronic Health Evaluation II) and pre-existing hypertension.

Khajavikhan et al. (2016) recommends using a glycemic control protocol for lowering blood glucose in patients with TBI in order to improve their outcome but cannot recommend a specific blood glucose target. Oh et. al. (2019) could also not recommend a specific target range of blood glucose for glycemic control in this group but advise that the previously mentioned factors should be adequately considered, especially during the first 72 hours.

6.6 Treatments and other factors that affect blood glucose

Treatments and other factors that affect blood glucose include four subthemes: Medications, Haemodialysis, Nutrition and Gender.

6.6.1 Medications

The use of Corticosteroids is, according to both Oh et al. (2019) and Becker et al. (2020) a large factor contributing to developing SIH. Becker et al found it to be the largest risk factor for suboptimal glycemic control, following DM. However, Becker et al. (2020) also found catecholamine infusions seem to play a role, but describes it as relatively small in comparison to DM and steroid use. Opposite to that, Crespo, Gomes, Barbosa, Padilha and Secoli (2017) found a higher prevalence of hypoglycemia in a group of patients on catecholamines.

Another medication that has been studied, but not nearly as widely, in this context is Magnesium. A study by Heidary, Khalili, Mohammadi, Beigmohammadi and Abdollahi (2020) found that a magnesium loading dose in patients with SIH improved glucose control, suggesting magnesium levels may play a part in insulin resistance.

6.6.2 Haemodialysis

Haemodialysis is considered a risk factor for developing hypoglycemia. This is described by Johnston et al. (2017) and further emphasised and investigated by Crespo et al. (2017), who contributed this phenomenon to the composition of the haemodialysis solution, filtration, and diffusion during the procedure and also to insulin resistance connected to uremia. Hypoglycemia was prevalent in both patients who received and did not receive insulin but was higher in those who did. They also showed that hypoglycemia was related to an increase in glycemic variability and mortality. Because of a strong association between hypoglycemia and death, Crespo et al. (2017) recommends the use of a protocol for glucose control, and specifically to prevent hypoglycemia and to identify patients at risk. Higher blood glucose targets and frequent measurement are also recommended by the authors.

6.6.3 Nutrition

According to different studies, a lack of nutrition could lead to both hypoglycemia (Crespo et al., 2017) and hyperglycemia (Oh et al., 2019). This is explained by Crespo et al. who found that the absence of an oral diet was a risk factor for developing hypoglycemia in critical care, since an oral diet brings metabolic stability compared to not being able to eat. Treskes et al. (2019) describes a lower and more variable insulin sensitivity on the first day, and especially during the first 12 hour of their ICU stay among critically ill patients who receive nutrition. A negative correlation was found between patients' caloric intake (enteral nutrition) and total serum insulin, while a positive was found between patients´ caloric intake and insulin resistance.Further, while the patient receives more calories, insulin resistance increases, leading to increasing need of exogenously administered insulin doses in order to maintain normoglycemia. When insulin resistance decreases, while aiming to reach a patient's nutritional target, the consequence cannot be predicted. Not only because of the inter- and intra-patient variability of SIH in the beginning of ICU stay, but also because during the acute phase, when

the stress response starts to decline, insulin resistance decreases as well. This rapid decrease in insulin resistance and higher glucose variability markedly increases the risk of hypoglycemic events because of insulin overdosing. (Treskes et al., 2019)

Considering all this, Crespo et al. (2017) therefore recommends attentiveness during glucose control, as does Oh et al. (2019) who advises consideration to nutrition and other influencing factors, while Treskes et al. (2019) recommends, during the first 24 hour of critically ill patients' treatment, restriction of the nutrition dose. A cautious dosing of insulin, higher blood glucose target and frequent blood glucose measurement to prevent hypo-, hyperglycemia and glucose variability was also recommended (Treskes et al., 2019).

6.6.4 Gender

Contradictory information can be found regarding BG and gender. For example, Oh et al. (2019) found that women were more likely to have high blood glucose levels. In addition to this Uyttendaele et al. (2021) found women to be more insulin resistant than men. Uyttendaele et al. explains the difference between men and women as a variation in metabolic stress response, meaning females respond more intensely to stress, resulting in higher insulin resistance. They describe the clinical significance as women possibly requiring higher doses of insulin to reach target glucose levels in glycemic control. Meanwhile, Johnston et al. (2017) found that female patients were at a higher risk for developing hypoglycemia, although Uyttendaele et al. found no difference between men and women regarding the risk of blood glucose lowering treatments.

7. DISCUSSION

The discussion part of this paper is divided into two parts. The first part; discussion of methods, explains the methods used to conduct this study and weighs any advantages and disadvantages connected to it. The second part; discussion of results, compares the results of the scoping review to other existing research and applies it to clinical nursing.

7.1 Discussion of methods

The discussion of methods is divided in the same manner as the method description: Design, Sample, Data collection and Data analysis.

7.1.1 Design of the study

This study is a scoping review. Scoping reviews are described by Pham, et al. (2014) as an approach that is relatively new but increased in popularity during the last few years. They identified a lack of agreement in methodology appropriate for this type of study, which was identified by the authors of this study as problematic. Therefore, the methodology used was based on descriptions of systematic reviews but omitting some steps that would have made it more systematic.

7.1.2 Sample

The chosen articles were, as previously stated, exclusively written in English, articles written in Swedish, and Spanish were also considered but were excluded for other reasons. Initially the plan was to not exclude any studies based on the design, although due to the nature of the research subject, only quantitative studies were found to match the aim of this study.

Henceforth, the studies analysed in this literature review were of different designs, meaning the data could be of varying quality, as some are of prospective design, only one used a RCT design, and most surveyed data only from medical records retrospectively. This gives the data used very different grades of quality. According to Worster, et al. (2004) a considerable amount of emergency medicine literature are retrospective studies based on review of medical records. They also describe a varying quality in these types of studies. The number of study participants varied from 24 to 6287 in the studies included in the analysis, resulting in a total of 17912 participants, making the mean number 1120, and median 239. Further, this study involved review of some case studies. Single case studies are described by Zainal (2017) as unable to generalize, unless they are used to research a phenomenon that is impossible to replicate. This might draw down the transferability of this study. The authors of this study are aware of this and after some consideration, decided to still include these studies as they still contribute to the result in a satisfying way.

The authors decided to also include articles that refers to the relative hyperglycemia (the stress hyperglycemia ratio (SHR)) which is a formula that can spot patients been at an increased risk of critical illness even though they are under the usually recommended values for starting treatment to lower blood glucose levels (Roberts et al., 2015).

The fact that the studies originated from a total of 11 different countries in 5 different continents gives this paper a global perspective but might make it difficult to generalize results and apply them to specific national circumstances, e.g., a higher responsibility of the specialist nurse in Sweden. The information may be possible to use anywhere in the world, but the part where the information is applied to the situation of the Swedish specialist nurse may be less generalizable because of the possibility of differing responsibilities as compared to situations in other parts of the world.

7.1.3 Data collection

There are strict requirements for inclusion criteria and strategy in data collection when conducting a systematic review (Snyder, 2019), therefore this paper is not considered a systematic review. The results from this study should still be reliable since the data is collected from multiple studies examining similar phenomena. Data collection was done according to the best of the authors knowledge, using the boolean operators AND and OR, to widen and limit the search, according to the description by Polit and Beck (2017). Truncations were also used to widen the search and catch any differing conjugation of words. As previously stated CINAHL and Pubmed were the databases selected for the data collection of this study. CINAHL, through search engine EBSCO, was chosen because Polit and Beck describes it as one of the main databases for finding nursing research, and Pubmed was chosen because it is a search engine to find most biomedical citations, as stated also by Polit and Beck.

Data collection was done in each of the separate search engines by one author each, which sped up the process but could also be limiting as different views and opinions may have played a role during this process.

7.1.4 Data analysis

To avoid bias and missing key points, data analysis was performed by the authors together according to previous description. Recommendations on this matter seem to vary, according to Polit and Beck (2017), as some recommend a single team member to code the entirety of data

to make sure it is consistent, while others recommend coding the data as a team. They also describe enhancing reliability by having two or more authors code at least some of the data, which is what was done for this study but, instead, both authors coded the entirety of the data.

7.2 Discussion of results

The aim of this study was to illuminate nurses´ strategies to enhance health and well-being through glycemic control in critically ill patients. This was done through summarizing and categorizing research in managing SIH, followed by applying the results on clinical practise.

The themes found in the results of this study is thought to be contributing to development of specialist nurses' connoisseurship by applying them during glycemic control. Meaning when evaluating the blood glucose value from a blood sample, consider these factors when (or before) initiating or re-evaluating treatment. Thus, contributing to good and safe glucose control, which will result in increased patient safety and quality of care.

Even though there are several important aspects and factors to consider while nursing patients with the mentioned diseases, we focused on glycemic control.

7.2.1 COVID-19

In the study by Ilias et al. (2020) 20 out of 36 study-participants without a history of DM had higher blood glucose values than expected during their stay in the ICU. As previously mentioned, a lot of evidence shows that hyperglycemia negatively affects the human body and has negative effects on patients' outcomes. The fact that a critically ill patient, that has Covid-19, may develop even higher blood glucose level due to the link with Covid-19 effect on hyperglycemia, should be considered for the specialist nurse. This information could be used while developing a safe and person- centered glycemic control strategy. The specialist nurse may need to administer a higher insulin dose to achieve normoglycemia, as well as frequent blood glucose levels measurement. At the same time, the risk for negative consequences of this treatment should also be kept in mind. Both, to avoid hypoglycemia and close blood glucose monitoring is recommended by accumulating empirical evidence as well as in some of the articles analysed in this work (Treskes, et al., 2019; Wernly, et al., 2019; Oh, et al., 2019).

Ilias et al. (2020) also describe how infectious complications may arise from hyperglycemia in critically ill patients. This is further explained by McCowen, et al. (2001) who reviewed several other studies that found a connection between hyperglycemia and complications in the form of infections. This mentioned connection and the elevated incidence of secondary infections presented for patients with Covid-19, as expressed by Ripa et al., (2020) are relevant and should be considered. If not, the patient may also be exposed to higher risk of contracting infections due to hyperglycemia because of unsuccessful glycemic control. This is where the importance of this complicated task becomes apparent. To achieve safe and good glycemic control, the mentioned aspects are - some of - the important elements for the nurse to take into consideration. Those elements should be combined and applied in person centered care. This is not just relevant for the patient but also for the specialist nurse to be considered as part of the "know-that" to be applied in clinical practice (knowing how) while developing connoisseurship.

7.2.2 Sepsis

Wernly et al. (2019) finding regarding glucose deviation increasing ICU and long-term mortality is supported by findings in other studies. For instance, Silveira et al. (2017) found that glycemic variability among non-survivors was greater than in survivors. A review by Plummer and Deane (2016) also found an association between glycemic variability and increased mortality. The specialist nurse could be aware of this and through a person centered approach and connoisseurship provides careful, safe, and good glycemic control. Treating the patient in a way that minimizes or, if possible, avoids that the patient's blood glucose values pendulates between hyperglycemia and hypoglycemia, promotes the patient´s health and well-being. This becomes an important task, since by succeeding in doing that, the specialist nurse could minimize the risk of exposing the patient to suffer from negative effects of glycemic variability and give good and safe care, as well as develop their own skills in the interim.

The reason for hyperglycemia related to sepsis is described by Hirasawa, Oda and Nakamura (2009) as metabolic changes in the body, because of both pro-inflammatory and anti-inflammatory responses caused by the infection. These metabolic changes result in negative effects on, among other things, the immune system which debilitates the host's ability to fight the infection (Hirasawa, et al., 2009). This is also pointed out by Ilias, et al. (2020). The negative effect on infections, together with the high prevalence of hyperglycemia in patients with sepsis shown by Treskes, et al. (2019), could negatively affect patients' health. Thus, this correlation

is also important to be considered for the specialist nurse while developing her glycemic strategy in order to not expose the patient to an increased risk of infection. A systematic review and comprehensive meta-analysis from Yao, et al., (2020) showed that several RCT studies found a decrease in the incidence of infections (including those that could lead to sepsis) while applying intensive glucose control. However, a higher prevalence of severe hypoglycemic events was found when comparing intensive glucose control to moderate glucose control. This is an important fact for the specialist nurse to consider as it may affect patients' health and well-being negatively and put patient safety at risk.

Findings in the study by Waeschle, et al. (2008), goes in the same line but the authors also showed that the degree of sepsis affected the risk of hypoglycemia negatively, despite having a higher blood glucose target. This knowledge could help the specialist nurse in giving good and safe care by being aware of different possible scenarios related to glycemic control.

Due to the high prevalence of hyperglycemia in patients that have sepsis it is most likely that the specialist nurse treats the patient with exogenous insulin to achieve normoglycemia. Further, as a result of the decrease in the previously mentioned peak in insulin resistance, the specialist nurse may need to decrease the insulin dose and closely monitor blood glucose concentration. Yet another part of the glycemic strategy is to keep in mind that a decrease in IR plus glycemic variability (Treskes et al., 2019) could result in hypoglycemia. This knowledge could give the specialist nurse a hint about how serum blood glucose levels could develop in relation to the degree of sepsis and the time from arrival. This knowledge, paired with connoisseurship and application of a person-centered approach, increases patient safety and quality of care.

7.2.3 Diabetes Mellitus

The results of the study by Wernly et al. (2019) that associated glucose deviation with increased ICU and long-term mortality in patients with and without DM, is supported by Alves Baptista, Felipe Felix, Oliviera de Souza, da Paixão Duarte and da Silva Magro (2018), who found that the worst outcome for patients was related to altered glucose values**.** They stated that variation in blood glucose level - and blood pressure - increases the risk for kidney injury, thus recommended to avoid pendulating blood glucose values (Alves Baptista et al., 2018; Sadaat-Gilani, Zarbock & Meersch, 2020). Alves Baptista et al. also lifted the fact that if the patient does not receive an effective and especially safe glycemic control, death could be the outcome.

Being one of the few studies that directly point out the importance of the specialist nurse's role in the mentioned regards. Not only in providing effective and safe glycemic management but also in collaborating to increase patient survival to safeguard good quality of care (Baptista et al., 2019). This enhances the clinical importance of a specialist nurse's connoisseurship in nursing practice and how it directly affects patients' outcome and quality of care.

Hyperglycemia has been linked with negative outcomes for patients with and without DM in the perioperative setting, and its treatment is strongly recommended according to a review (Chen & Duggan, 2019). But Wernly et al. (2019) did not find an increase in mortality (ICU or long term) in patients with T2DM even though they found a higher prevalence of severe hyperglycemia in these patients. This "know-that" could mean for the specialist nurse that hyperglycemia should be treated and avoided in all patients but also to be aware that patients with T2DM have an increased risk for developing hyperglycemia and receiving suboptimal glycemic control. Individualised targets for glycemic control should be adapted to treat hyperglycemia considering, for instance, if the patient has DM (Chen & Duggan, 2019).

But it is not just glycemic deviation and hyperglycemia that the specialist nurse should avoid considering patients' well-being and safety. A study by Ndebu and Jones (2018) found that incidence of hypoglycemia was higher during night-time than daytime, both in critical care and in-patient wards. They also found there was a discrepancy in what blood glucose values were considered hypoglycemic, which ranged from 2.5 mmol/l to 4.0 mmol/l. This is a problem since Wernly et al (2019) also found that already one hypoglycemic event, resulted in increased ICU and long-term mortality, both in patients with and without DM. Showing and recommending that hypoglycemia should be avoided in all patients, since it puts patients' life at risk. This is an important factor that should be part of specialist nurse connoisseurship to give good and safe care. This also relates to the fact that it seems to be difficult to draw conclusions on target range when it comes to glycemic control (Kar et al., 2016) and a solution might be, as suggested by Wernly et al. (2019), to individualise blood glucose targets for diabetic patients, which is supported by Shea, Gerard and Krinsley (2019) who used a different glucose control protocol for diabetic/non-diabetic patients.

In order to not risk patient well-being and safety, all these different facts, among others, should be carefully considered and combined for the specialist nurse while developing glycemic strategies through her connoisseurship.

7.2.4 Cardiology

All the analysed articles connect in different ways that high blood glucose values, referred to as SIH or SHR, affect cardiac patients' health negatively leading to negative outcomes. Some studies have stated that this negative impact is more pronounced in patients without DM than in those with DM (Kojima et al., 2020; Wernly et al., 2019). A study by Greco, Kirkwood, Gelijns, Moskowitz and Lam (2018) found a three-way interaction between DM, stress hyperglycemia and hyperglycemia linked with patients´ mortality after cardiac surgery. The authors showed that DM may serve protective, in the acute phase of the disease, against postoperative hyperlactatemia (Greco et al., 2018) and against hyperglycemia (Wernly et al., 2019).

According to a big body of literature, in this group of patients, it is also important to avoid hypoglycemia (Stoudt & Chawla, 2019; Koraćević et al. 2020) and glycemic variability (Stoudt & Chawla, 2019; Alatawi & Mirghani, 2020) to protect patients of its negative outcomes. This is in the same line as Johnston et al. (2017) findings, who recommends being especially careful when a patient presents both hypo- and hyperglycemia. Further on, hypoglycemia should also be avoided, even by permitting mild hyperglycemia, although no glucose value was specified in their recommendations.

Back in time, as mentioned, the Leuven study postulated in 2001 that tight glycemic control reduced mortality in critically ill patients. This changed in 2009 starting with the NICE-SUGAR study showing instead a considerable increase in mortality following the tight glycemic control, because of hypoglycemia due to the narrow blood glucose targets. After accumulating empirical evidence, more conservative and liberal targets were recommended around the world. But recent research shows that particularly in this patient population, a stricter blood glucose target to treat hyperglycemia seems to be the best and safest approach (Stoudt & Chawla, 2019; Landoni et al., 2018). Stoudt et al. pointed out in a review that cardiac surgery patients may have improved outcomes with tighter glycemic control. For the rest of the population, they recommend a moderate approach with blood glucose values between 7.8 and 10 mmol/L. This information greatly enhances the importance of a person centered approach in the specialist nurse’s care of critically ill patients, specifically those admitted for a cardiac condition. Especially since evidence indicates this is the proper route to take. The practice of a person centered care in this regard will also add to the nurse’s connoisseurship and contribute both, to the development of the nurse’s clinical expertise and to increase patient well-being.

According to a review published in 2020 (Scheen, Giraud & Bendjelid, 2020), some paradigms are changing and a phenomenon that is called glucotoxicity, could explain the benefits of having lower glucose values in these patients could improve heart function and positively affect patients' recovery. According to Meshref et al., (2020), in STEMI patients, hyperglycemia is positively correlated with the myocardial area at risk and the final infarct size. Thus, they stated that strict glucose control is very important in the acute phase of STEMI.

Javaherforoosh zadeh and Azemati (2017) found in their study comparing tight vs "conventional" glycemic control in patients undergoing CABG (Coronary Artery Bypass Graft) surgery no difference in mortality or hypoglycemic episodes between the two groups. However, they did find that the rate of infection was lower in the tight glycemic control group. A significant difference in mortality was, however, found in a study by Hersh et al. (2018), who found that mortality was lower in cardiac and cardiothoracic patients treated with a tighter blood glucose range. The difference in hypoglycemic rate on the other hand was not significant between the tight and conventional group (Hersh et al., 2018). Hypoglycemia is what Johnston et al. (2017) found contributed considerably to the high mortality and is supported by the finding by Kataja et al. (2016).

The specialist nurse could take this knowledge and apply it in the clinical practice to enhance patient safety. It is vital that the specialist nurse builds up her connoisseurship with the latest evidence-based care data. Due to the impact that glycemic control has in critically ill patient outcomes and considering the important role that specialist nurses have. The different approaches that should be taken in the different patient populations, as was discussed above, should be considered and be part of a nurse's connoisseurship. Doing so may benefit both the nurse and the patient. Through an increase in connoisseurship, the quality of care may also increase, opening the doors for a more person-centered and safe care.

7.2.5 Brain injury

Chen et al. (2019) found a significant association between stress hyperglycemia and negative outcome in non-diabetic stroke patients. This relates to the findings in the articles analysed in this scoping review by Oh et al. (2019) and Khajavikhan (2016) who both could connect poor outcomes with hyperglycemia in patients with brain injury.

In a review by Hermanides et al. (2018), no difference in mortality was found between intensive and conventional glucose control among patients with TBI. Similar results were found in

another review by Zhu, Chen, Pan, Qiu and Xu (2018). However, Zhu et al. did find that intensive glycemic control seems to serve protective in improving neurological outcome, reducing infection rate and length of stay in the ICU. Studies included in Hermanides et al. review used different target ranges, with intensive glycemic control aiming for 4.4-6.7 mmol/l and the target range in the conventional groups varying highly between 8.4 to 12 mmol/l being the higher target (Hermanides et al. (2018). Because of these findings, no conclusion to treat patients with TBI different from other critically ill patients was drawn by Hermanides et al. This relates to the conclusion Khajavikhan et al. (2016) and Ye et al. (2020) drew, meaning no specific target range was recommended, as well. Even though no difference in mortality was observed in the mentioned studies, it has, however, been observed that keeping blood glucose within normal range values serves neuroprotective. When the specialist nurse's care in this group of patients strives toward neurological recovery it directly affects the patient's health as the future daily function of the patient is dependent on neurological function. It becomes evident in these patients that surviving is not the only goal to aim for. Preserved neurological function might be just as important, and glycemic control seems to be one of several crucial elements to consider that has been shown to impact this.

Mongkolpun, Provenzano and Preiser (2019) found in their review that keeping blood glucose in the upper normal target range during the first week after brain injury, followed by a tighter glycemic control in the second week was beneficial regarding both neurological outcome and survival rates. They also point out the fact that patients with brain injuries are more susceptible to hypoglycemia and sensitive to glycemic variability compared to other groups of patients, because of a smaller glucose reserve.

Even though no target ranges are recommended, we know that the mortality in these patients, as well as the neurological outcome, are negatively affected by hyperglycemia. Furthermore, these patients also react negatively to blood glucose variations. This makes it important to keep these patients' blood glucose values, at least initially (during the first week), within the higher spectrum of normal target range, followed by a tighter glycemic control from week two after the onset of brain injury.

This is important knowledge for the specialist nurse to keep in mind when caring for these patients, especially if a standardised protocol (or none) for glycemic control, is used in their unit. Also, studies advise a personalised approach, taking affecting variables, such as use of steroids, calorie intake, gender, APACHE II score and hypertension, into consideration. The

expert specialist nurse may take these different variables and be able to calculate an appropriate intervention for the hyperglycemia that the patient is presenting. The person centered aspect of this would be to apply suitable factors that are affecting glycemic regulation in this specific patient. This, combined with adjustments according to the time frame, might both positively affect patient safety along with patient outcome, but will also be useful for the nurse when developing their connoisseurship and aiming to reach expert level.

7.2.6 Treatments and other factors that affect blood glucose

The four previously mentioned subthemes are discussed one at a time, in the same manner as the results are presented.

7.2.6.1 Medications

According to Svensk sjuksköterskeförening (2020) the swedish intensive care specialist nurses have specific knowledge in safely administering and evaluating treatment, as well as knowledge about the effects and side effects. Corticosteroids are found to be a major contributing factor to develop hyperglycemia in the critically ill (Becker et al., 2020; Oh et al., 2019), but catecholamines are pointed out as well (Becker et al., 2020). Becker et al. seems to relate this more to the use of Epinephrine compared to Norepinephrine, which is something to keep in mind, especially for nurses who work in a setting where Epinephrine is more commonly used. Such an area of work might be a ward where patients are cared for post cardiac surgery (Becker et al., 2020). According to Russel et al. (2021), however, Epinephrine is also commonly used in countries where Norepinephrine is more expensive, alternatively complimentary to Norepinephrine if it is not enough to reach hemodynamic stability.

Godinjak et al. (2015) did not study the association between blood glucose and vasopressors or corticosteroids, but rather recommended intravenous insulin infusion for these patients. The reason for intravenous insulin being recommended for patients in the ICU is because of the unforeseeable rate of absorption of oral and subcutaneous medication that is associated with hypotension and shock. These conditions are common causes for admission to the ICU as well as a reason for the use of corticosteroids and catecholamines (Bağır & Ertörer, 2017).

As previously described, a lot of evidence exists suggesting the use of a protocol for glycemic control using intravenous insulin. Protocols are in place to treat hyperglycemia, and paired with frequent blood glucose measurements, decrease hypoglycemic events. This is a tool for the

specialist nurse to deal with glycemic control and is important for patient safety in a setting where the patient is unable to express signs and symptoms of hyper- and hypoglycemia. In a study by Ndebu and Jones (2018) however, signs of hypoglycemia were not common knowledge for nurses working in the ICU. Although that study was conducted in the UK, the results enhance the importance of the swedish intensive care specialist nurses' specific knowledge in this field of work. Especially considering the substantial responsibilities that they have. The importance of a person centered approach becomes evident when patients not only present different diseases and conditions, but also are being treated with varying medications that affect the patient's blood glucose. On top of this they may also respond to these drugs differently. Another important factor is that if the patient is sedated or anesthetized, hypoglycemia may be difficult to detect without taking a blood gas and the patient could in the worst case, die.

Over time, while developing their skill towards the connoisseurship of the expert, the nurse will gain experience and learn to recognise how different patients respond to different doses of insulin while titrating the medication. This knowledge will enhance PCC and increase patient safety.

7.2.6.2 Haemodialysis

Vriesendorp et al. (2006) as well as Stevenson et al. (2013) could, just like Johnston et al. (2017) and Crespo et al. (2017), find a correlation between renal replacement therapy (RRT) and hypoglycemia, although they could also find a correlation between the risk of hypoglycemia with the type of substitution fluid used during this time. Vriesendorp et al. could only find an increased risk of hypoglycemia among the patients on bicarbonate substitution fluid, and not among those who received a substitution fluid that was lactate-based. Stevenson et al. found that the filtration rate and the pre-filter blood glucose had an impact on glucose removed during CRRT.

This is a factor for the specialist nurse to consider when caring for critically ill patients who need haemodialysis, as nutrition rate might need adjustment in order to prevent loss of calories (Stevenson et al., 2013), as well as adjustment in insulin infusion rate in order to prevent hypoglycemia. Iyengar, Franzese and Gianchandani (2018) reviewed several studies and found that a reduction in insulin doses were required on the days patients received haemodialysis. This finding regards both hospitalized and not hospitalized patients on intermittent dialysis but

is worth remembering for intensive care patients as well since they generally are clinically sicker. This knowledge can be used for the specialist nurse to know to adjust blood glucose lowering treatments to prevent hypoglycemia, due to RRT. It can be seen as part of a person-centered approach as well as preventative care, which is a component in health promotion. This might directly affect patient outcome, as the risk of hypoglycemia, with its possibility to lead to negative events, decreases. Patient safety and health will therefore increase, as well as the specialist nurses' "know-that" and connoisseurship, which is a mutually beneficial situation.

7.2.6.3 Nutrition

The contradictory results regarding nutrition and both hyper- and hypoglycemia make nutrition especially difficult, but largely important, for the specialist nurse to acknowledge when they care for the critically ill patient. Van Zanten, De Waele and Wischmeyer (2019) recommend a careful titration of nutrition during the initial phase of intensive care, in line with Treskes et al. (2019) recommendation. This recommendation by Van Zanten et al. is partly because of the risk of hyperglycemia, but also because of the risk of refeeding syndrome. Miller, et al. (2020) found that eating while on continuous insulin infusion did increase the variability of the blood glucose, compared to patients who did not eat, but were unsure of the clinical relevance of this finding. Generally, in an ICU-setting, the patients are clinically too sick to be able to eat on their own, and when they are well enough to do so they might no longer require IIT. But for the occasions that this happens it is important knowledge for the specialist nurse to consider.

Kavanagh and McCowen (2010) found that the difference in outcome between the two major studies investigating IIT may have been due to a different approach to nutrition. Therefore, nutrition needs to be taken into consideration during IIT in intensive care, along with the findings by Crespo et al. (2017) and Oh et al. (2019). These results can be enhanced with the recommendation by Treskes et al. (2019) which included cautious insulin dosing, higher target blood glucose and frequent measurement of such.

In general, enteral feeding is recommended, as it stimulates the intestines and lowers the cost while also eases intravenous access (Koekkoek & van Zanten, 2017) which can be used for other purposes. On one hand enteral nutrition is favourable, because of the mentioned reasons, but on the other hand it might be problematic considering the careful titration that is required due to the possibility of retention of nutrition formula in the stomach. Koekkoek and van Zanten also enhance the importance of not under- or overfeeding the patient, as it is suggested that both

result in adverse outcomes. A correct approach to nutrition is therefore a crucial part of the specialist nurse's practise as it may decrease the risk of adverse outcome. As these adverse outcomes may result in patient suffering, preventing it may be seen as directly health promoting work.

Nutrition is a perfect practical example as to why PCC is so important. Different sized people, with different body compositions and health status require different amounts of calories and nutrients and is therefore an aspect that the specialist nurse must consider.

7.2.6.4 Gender

Mauvais-Jarvis (2019) explains in a review that women present the same levels of fasting blood glucose as men, but the blood glucose increased more in the female population during oral glucose tolerance test. They relate it to the fixed dose of glucose used during these tests, in relation to height and body composition, as they also found that the glycated haemoglobin in women was almost identical to men. Sicree et al. (2008) however found height to be the biggest contributing factor to this phenomenon.

Uyttendaele (2021) found that insulin resistance increased in women during metabolic stress, while Mauvais-Jarvis (2019) means that when not under stress, women are just as sensitive to insulin, if not more, than men. This could explain why Johnston et al. (2017) found that women are more prone to hypoglycemia than men. When women require more insulin to reach blood glucose targets during stress, and then the stress response decreases, the higher dose of insulin would cause the blood glucose to drop hastier. Mauvais-Jarvis further explains that estrogen levels could contribute, but also found that fitness levels played a part in glucose homeostasis in women. Mohr et al. (2010) found that blood glucose variability in women did not increase mortality to the same extent as it did in men. This suggests that, though women are more likely to be hyperglycemic (Oh et al., 2019), hypoglycemic (Johnston et al., 2017) and require higher insulin doses to achieve desired blood glucose value targets (Uyttendaele et al., 2021), it may not affect the mortality rate.

While the mortality might not increase in women with glycemic variability, as stated above, it might have other effects that have not been discussed in this context. One example of another negative event caused by hyperglycemia is increased risk of secondary infections, as previously discussed. This fact alone elevates the important task of the specialist nurse that is glucose control and should not be disregarded. Secondary infections may increase the ICU- and hospital

length of stay, which consecutively potentially increases the risk of unnecessary suffering for the patient. To minimise suffering in this way highlights both the fundamental responsibility of the nurse, as well as the specific role of the intensive care specialist nurse that is to analyze vital functions and initiate and evaluate treatment accordingly (Svensk sjuksköterskeförening, 2020). This, in turn, relates to Brykczynski (2010) explanation of clinical nursing through Benner's theory. She states nurses respond accordingly to a given situation and its demands through the perceptual awareness that is acquired with experience in nursing (Brykczynski, 2010).

In summary, the specialist nurse may require different insulin dosing for women compared to men to reach the same goal, therefore a personalised approach is advised, and is useful as a step for the nurse towards reaching connoisseurship in nursing.

8. CONCLUSION

It remains controversial among researchers whether tight glycemic control or a less strict approach is safest. Data suggests that a person-centered approach, considering different patient populations should be applied to glycemic control in order to safeguard critically ill patients' health and safety. The importance of a protocol to help nurses in the complex task of glycemic control is advised as a part of the nurse's strategy.

8.1 Clinical implications

This study may be beneficial for both the specialist nurse and the patient. It may increase nurses' possibility to apply a more person-centered approach to glucose control, while helping them to increase their connoisseurship and the development of clinical expertise. Thus, enhancing patients' health and well-being by giving qualitative care while safeguarding patients' lives.

8.2 Future research

More research, at a larger scale than is available today, should be done focusing on the best recommended nurses' glycemic control strategies in critically ill patients. This could be based on how different factors and inter- and intra-patient differences affect blood glucose management. This could facilitate that complex task, increase PCC and safe and quality care.

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APPENDIX

Appendix 1 – Search Matrix

Date	Database	Search term	Limiting factors	Hits	Abstracts read	Selected studies, nr (double)
14/3	CINAHL	Stress hyperglycemia AND critica* ill OR critical care AND Nurs* AND glucose control	2016-2021, English, Research article, Peer reviewed	40	25	(4), (10),
15/3	CINAHL	Stress hyperglycemia OR stress induced hyperglycemia OR SIH AND Nurs* AND Glucose control	2016-2021, Peer reviewed	70	30	9, (4), 8, 11, (7), 15
1/2	PubMed	Nursing[MeSH Terms] OR Nurs* AND "glycemic control" OR "glycaemic control" AND critical* ill OR critical care[MeSH Terms]	English, Humans, Publication last 5 years	27	14	1, 10
22/2	PubMed	critica* ill AND "glycemic" OR "glycaemic" OR blood glucose[MeSH Terms] OR "blood glucose" (free text)	English, Humans, Publication last 5 years	192	69	12, 13, 2, 3
25/2	PubMed	"stress induced hyperglycemia" OR "SIH" OR "stress induced hyperglycaemia" AND critica* ill OR "critical illness" OR "critical care" AND nurs*	same than above	5	2	7
10/3	PubMed	same as above but without nurs*	same as above	27	19	(1), (4), (7), 8
10/3	PubMed	stress hyperglycemia AND critica* ill OR "critical illness" OR "critical care" stress hyperglycemia AND "critically ill" OR "critical illness" OR "critical care"	same as above	119	44	(1), (2), (3), 4, 5, 6, (7)

Appendix 2 – Article Matrix

Nr	Author, (year), titel, *journal*, country	Aim	Method	Conclusion
1	Treskes, N., Koekkoek, W., & van Zanten, A. (2019). The Effect Of Nutrition on Early Stress-Induced Hyperglycemia, Serum Insulin Levels, and Exogenous Insulin Administration in Critically Ill Patients With Septic Shock: A Prospective Observational Study. *Shock.* Netherlands.	To determine the course of hyperglycemia and serum insulin levels in critically ill septic shock patients and to address the effects of caloric intake on glycemia, insulin levels, and exogenous insulin requirements.	A prospective, observational study of 24 ventilated septic shock patients during 72 h after ICU admission.	Frequent glycemic monitoring, conservative insulin, slow progressive nutrition.
2	Ilias, I., Jahaj, E., Kokkoris, S., Zervakis, D., Temperikidis, P., Magira, E., Pratikaki, M., Vassiliou, A. G., Routsi, C., Kotanidou, A., & Dimopoulou, I. (2020). Clinical Study of Hyperglycemia and SARS-CoV-2 Infection in Intensive Care Unit Patients. *In vivo (Athens, Greece).* Greece.	To describe the course of glycemia in critically ill patients with severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection.	Prospective observational study of 36 non-diabetic COVID-19 patients in the ICU with hypoxemic respiratory failure.	A substantial number of patients had hyperglycemia, to a higher degree than would be expected by the stress of critical Illness.
3	Wernly, B., Jirak, P., Lichtenauer, M., Franz, M., Kabisch, B., Schulze, P. C., Braun, K., Muessig, J., Masyuk, M., Paulweber, B., Lauten, A., Hoppe, U. C., Kelm, M., & Jung, C. (2019). Hypoglycemia but Not Hyperglycemia Is Associated with Mortality in Critically Ill Patients with Diabetes. *Medical principles and practice : international journal of the Kuwait University, Health Science Centre.* Germany	To investigate associations of a single episode of blood glucose deviation during an ICU stay with mortality in these patients.	4,986 patients admitted to a German ICU were investigated retrospectively based on medical records.	In patients with diabetes, hypo- but not hyperglycemia was associated with increased mortality, whereas in patients without diabetes, both hyper- and hypoglycemia were associated with adverse outcome.

Nr	Author, (year), titel, *journal*, country	Aim	Method	Conclusion
4	Heidary, Z., Khalili, H., Mohammadi, M., Beigmohammadi, M.-T., & Abdollahi, A. (2020). Effect of Magnesium Loading Dose on Insulin Resistance in Patients With Stress-Induced Hyperglycemia: A Randomized Clinical Trial. *Journal of Intensive Care Medicine (Sage Publications Inc.).* Iran	To evaluate effects of magnesium loading dose on insulin resistance (IR) indices in critically ill patients without diabetes having SIH.	Double-blinded, placebo-controlled, randomized clinical trial including 50 consecutive non-diabetic patients with SIH in the ICU,	A single-loading dose of intravenous magnesium improved IR indices in critically ill patients with SIH.
5	Chan, M. C., Tseng, J. S., Hsu, K. H., Shih, S. J., Yi, C. Y., Wu, C. L., & Kou, Y. R. (2016). A minimum blood glucose value less than or equal to 120 mg/dL under glycemic control is associated with increased 14-day mortality in nondiabetic intensive care unit patients with sepsis and stress hyperglycemia. *Journal of critical care.* Taiwan	To investigate whether the minimum blood glucose value, during the first 72 hours after admission, was associated with mortality in patients with severe sepsis.	Retrospective analysis of prospectively acquired clinical data from 127 septic patients admitted to an ICU.	A blood glucose value less than or equal to 120 mg/dL was an independent risk factor for 14-day mortality in nondiabetic patients, but not in diabetic patients under the same setting.
6	Khajavikhan, J., Vasigh, A., Kokhazade, T., & Khani, A. (2016). Association between Hyperglycaemia with Neurological Outcomes Following Severe Head Trauma. *Journal of clinical and diagnostic research : JCDR.* Iran	To assess the correlation between hyperglycaemia with neurological outcomes following severe Traumatic Brain Injury (TBI).	Descriptive and correlation study, retrospective data collection through medical records of 83 patients.	Hyperglycaemia after severe TBI is associated with poor outcome.
7	Oh, H., Lee, K., Shin, S., & Seo, W. (2019). Temporal Patterns and Influential Factors of Blood glucose Levels During the First 10-Day Critical Period After Brain Injury. *Clinical Nursing Research*. Korea	To document temporal patterns of blood glucose level changes during the first 10-day critical period and to identify factors that influence stress-induced hyperglycemia development in brain injury patients.	Retrospective review of medical records of 190 braininjured patients in the ICU.	Close monitoring and adjustment are required to maintain safe blood glucose levels.

Nr	Author, (year), titel, *journal*, country	Aim	Method	Conclusion
8				SIH was associated with the occurrence of R-DWILs in patients with primary ICH within 14 days of symptom onset.
9	Meng, S., Zhu, Y., Liu, K., Jia, R., Nan, J., Chen, M., Lei, X., Zou, K., & Jin, Z. (2021). The stress hyperglycaemia ratio is associated with left ventricular remodelling after first acute ST-segment elevation myocardial infarction. *BMC cardiovascular disorders*. China	To assess the association between the stress hyperglycaemia ratio (SHR) and left ventricular negative remodelling.	127 first-time, anterior, STEMI patients were enrolled and divided into 2 sublood glucoseroups according to the median value of SHR level. Echocardiography was done within 24 h after admission and compared to 6 months post-STEMI.	SHR is signifcantly correlated with left ventricular negative remodelling after STEMI.
10		To determine hypoglycemia incidence and associated factors in critically ill patients.		
11	Qin, Y., Yan, G., Qiao, Y., Ma, C., Liu, J., & Tang, C. (2019). Relationship between Random Blood glucose, Fasting Blood glucose, and Gensini Score in Patients with Acute Myocardial Infarction. *BioMed research international.* China	To examine the relationship between admission random blood glucose (Rblood glucose), fasting blood glucose (Fblood glucose), and Gensini score in patients with acute myocardial infarction (AMI).	958 consecutive AMI patients who underwent emergency coronary angiography were enrolled. Gensini score of each patient was calculated according to the results of coronary angiography.	Gensini scores of patients in the stress hyperglycemia group and the elevated Fblood glucose group were significantly higher than those in the control group.

Nr	Author, (year), titel, *journal*, country	Aim	Method	Conclusion
12	Becker, C. D., Sabang, R. L., Nogueira Cordeiro, M. F., Hassan, I. F., Goldberg, M. D., & Scurlock, C. S. (2020). Hyperglycemia in Medically Critically Ill Patients: Risk Factors and Clinical Outcomes. *The American journal of medicine*. USA	To categorize glycemic control, identify clinical risk factors for suboptimal control; and compare clinical outcomes between the 2 glycemic control categories.	A retrospective cohort study of 920 patients in an ICU,	Average daily blood glucose levels <180 mg/dL significantly decreased the odds of subsequent hospital mortality. Suboptimal glycemic control during the ICU stay significantly increased the odds of longer ICU and hospital stay.
13	Uyttendaele, V., Chase, J. G., Knopp, J. L., Gottlieb, R., Shaw, G. M., & Desaive, T. (2021). Insulin sensitivity in critically ill patients: are women more insulin resistant?. *Annals of intensive care.* New Zealand	To determine if there are diferences in inter- and intra-patient metabolic variability between sexes in adults.	Insulin sensitivity levels and variability are identified and analysed from retrospective clinical data from GC episodes of minimum 24 h of 91 men and 54 women. .	Females can receive the same benefit from GC as males, but may require higher insulin doses to achieve the same glycaemia.
14	Johnston, L. E., Kirby, J. L., Downs, E. A., LaPar, D. J., Ghanta, R. K., Ailawadi, G., Kozower, B. D., Kron, I. L., McCall, A. L., Isbell, J. M., & Virginia Interdisciplinary Cardiothoracic Outcomes Research (VICTOR) Center (2017). Postoperative Hypoglycemia Is Associated With Worse Outcomes After Cardiac Operations. *The Annals of thoracic surgery.* USA	To examine the effects of postoperative hypoglycemia, hyperglycemia, and their interaction on short-term morbidity and mortality.	Retrospective review of 2285 patients' medical records.	Postoperative hypoglycemia is associated with both mortality and major morbidity after cardiac operations. The combination of both hyperglycemia and hypoglycemia represents a substantial increase in risk.

Nr	Author, (year), titel, *journal*, country	Aim	Method	Conclusion
15	Gao, S., Liu, Q., Ding, X., Chen, H., Zhao, X., & Li, H. (2020). Predictive Value of the Acute-to-Chronic Glycemic Ratio for In-Hospital Outcomes in Patients With ST-Segment Elevation Myocardial Infarction Undergoing Percutaneous Coronary Intervention. *Angiology.* China	To investigate whether an index of stress hyperglycemia might have a better prognostic value compared to admission glycemia in patients with STEMI undergoing PCI.	A total of 1300 consecutive patients with STEMI treated with PCI were retrospectively included through review of medical records.	Taken together, Ablood glucose/eAG provides more significant in-hospital prognostic information than Ablood glucose in diabetic patients with STEMI after PCI.
16	Kojima, T., Hikoso, S., Nakatani, D., Suna, S., Dohi, T., Mizuno, H., … Osaka Acute Coronary Insufficiency Study (OACIS) Group (2020). Impact of Hyperglycemia on Long-Term Outcome in Patients With ST-Segment Elevation Myocardial Infarction. *The American journal of cardiology.* Japan	To examine the association between SIH early after the onset and long-term prognosis in ST-segment elevation myocardial infarction (STEMI) patients discharged alive, and differences in the significance of SIH between diabetic and nondiabetic patients.	Prospective, multicenter observational study of 6287 consecutive patients with AMI at 25 collaborating hospitals.	Strong SIH, expressed as high SHR, was significantly associated with worse long-term prognosis in STEMI patients who were discharged alive, especially in those without DM.