Slovenian Medical Journal

Insulin resistance as a perioperative consideration and basis for enhanced recovery after cardiovascular surgery

Inzulinska rezistenca v perioperativnem obdobju – temelj večdisciplinarnih pobud za pospešeno okrevanje po posegu v srčnožilni kirurgiji

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Abstract

Insulin resistance, the state of reduced biological response to physiological levels of insulin, is a key risk factor for cardiovascular disease. Consequently, it frequently occurs in patients undergoing cardiovascular surgery. Inflammatory processes, tissue damage, and hormonal response in the perioperative period further contribute to insulin resistance, leading to various biochemical changes. These negatively affect organ functioning, postoperative complications and recovery after surgery. Insulin resistance manifests itself as a wide range of clinical conditions that gradually progress from hyperinsulinaemia to impaired glucose tolerance and finally overt hyperglycaemia; when normoglycaemia is no longer maintained despite increasing insulin secretion. The recommendations of various professional associations regarding target values of blood glucose in the perioperative period are not unequivocal. Breakthrough research has initially shown that strict glycaemic control leads to better outcomes, but the incidence of hypoglycaemia is an important safety consideration. Current protocols for perioperative insulin administration target glycaemic values between 7.8 and 10 mmol/L (140 to 180 mg/dL). Whether morbidity and mortality are affected by the degree of hyperglycaemia or the mere presence of diabetes or insulin resistance itself, remains to be elucidated. Insulin resistance in the perioperative period can be avoided with a minimally invasive surgical approach, optimal choice of anaesthesia and analgesia and with shortened periods of starvation. The present manuscript discusses the pathophysiology and clinical consequences of insulin resistance or hyperglycaemia, and describes perioperative strategies to reduce insulin resistance, selecting the best treatment options for enhanced recovery after cardiac and complex aortic surgery.

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Key words: diabetes mellitus; perioperative hyperglycaemia; insulin therapy; cardiovascular and major vascular surgery; enhanced recovery after surgery

Ključne besede: sladkorna bolezen; perioperativna hiperglikemija; inzulinsko zdravljenje; srčnožilne in velike žilne operacije; kirurgija s pospešenim okrevanjem

Received / Prispelo: 24. 9. 2020 | **Accepted / Sprejeto:** 10. 12. 2020

Cite as / Citirajte kot: Volčanšek Š, Kšela J. Insulin resistance as a perioperative consideration and basis for enhanced recovery after cardiovascular surgery. 2021;90(7–8):443–53. **DOI:** https://doi.org/10.6016/ZdravVestn.3164

Izvleček

Inzulinska rezistenca oziroma stanje zmanjšanega biološkega odziva na fiziološke ravni inzulina je ključni dejavnik tveganja za srčnožilne bolezni, zato je pogosto prisotna pri bolnikih v srčnožilni kirurgiji. Vnetni procesi, poškodba tkiva in hormonski odziv v perioperativnem obdobju dodatno prispevajo k inzulinski rezistenci, ki vodi v različne biokemične spremembe. Le-te negativno vplivajo na delovanje organov, na zaplete po operaciji in na okrevanje po njej. Inzulinska rezistenca se kaže kot širok nabor kliničnih stanj, ki se postopno razvijajo od hiperinzulinemije do motene tolerance za glukozo in končno hiperglikemije, ko se normoglikemija ne more več vzdrževati kljub povečanemu izločanju inzulina. Priporočila različnih strokovnih združenj glede ciljnih vrednosti krvnega sladkorja v perioperativnem obdobju niso enoznačna. Prelomne raziskave so sprva dokazale, da strog glikemični nadzor vodi do boljših izidov, vendar je pojavnost hipoglikemij pomemben varnostni zadržek. Zato se v danes uveljavljenih protokolih za perioperativno odmerjanje inzulina cilja na vrednosti glikemije med 7,8 in 10 mmol/l. Hkrati pa je nejasno, ali na obolevnost in smrtnost vpliva stopnja hiperglikemije ali že zgolj prisotnost sladkorne bolezni oziroma sama inzulinska rezistenca. Procesom inzulinske rezistence v perioperativnem obdobju se lahko izognemo z minimalno invazivnim kirurškim pristopom, ustrezno anestezijo ter analgezijo in skrajšanjem obdobij stradanja. Prispevek obravnava patofiziologijo in klinične posledice odpornosti na inzulin oziroma hiperglikemije ter opiše perioperativne strategije za zmanjševanje inzulinske rezistence, izbiro najbolj primernega načina zdravljenja in pristope za hitrejše okrevanje po posegu na srcu in po kompleksnih operacijah aorte.

1 Introduction

Perioperative hyperglycaemia has been reported in 20–40% of general surgical patients and in as many as 80% of patients after cardiovascular surgery (1,2). Metabolic changes that occur before, during and after surgery, including enhanced glucose production and impaired glucose uptake, lead to high blood glucose levels during this period. Many of these metabolic processes can be explained by the neuroendocrine changes that occur as part of surgery. These inhibit the secretion of insulin and/or prevent its peripheral action, which is called insulin resistance (3-6). The extent of insulin resistance and the metabolic response to surgery are related to the duration of surgery and its invasiveness. It depends on the extent of tissue damage, suggesting that insulin resistance is a marker of surgical stress (4). Independent of intraoperative stress due to tissue damage, blood loss also directly affects postoperative insulin resistance (5). Physical inactivity after surgery results in poorer glucose uptake in skeletal muscle. A caloric and protein-inadequate diet in the perioperative period can lead to a negative nitrogen balance, which affects the metabolic environment and increases insulin resistance (4). During cardiovascular surgery, insulin resistance and hyperglycaemia additionally occur as a result of the release of inflammatory cytokines through the use of extracorporeal circulation, the release of stress hormones due to cardioplegia or even circulatory arrest, moderate or deep hypothermia, and iatrogenic use of heparin and catecholamines (4,5). Thus, the stress of an acute or chronic underlying disease alongside a more or less aggressive and non-physiological surgery results in transient but reversible insulin resistance lasting up to 21 days after surgery (7).

HbA1c levels are known to predict insulin sensitivity during surgery and morbidity and mortality in cardiovascular surgery in patients with diabetes. Intraoperative insulin resistance itself is also significantly associated with an increased risk for complications, regardless of the patient's management of diabetes (8,9).

The perioperative mechanisms described in this article are characteristic of cardiac surgery (with or without extracorporeal circulation) and complex large vessel surgeries (such as thoracic and abdominal aortic surgeries, which may also be performed with or without extracorporeal circulation), but not for less complex vascular interventions (minor surgical procedures on infrarenal abdominal aorta or procedures on peripheral vascular system), as surgical injury and stress response of the organism to such operations are significantly lower.

2 Insulin resistance and glucose metabolism during surgery

Insulin resistance is defined as a reduced biological effect of insulin. With the onset of insulin resistance, normoglycaemia is achieved by increasing insulin secretion from pancreatic beta cells, resulting in hyperinsulinaemia (6). In the general population, this condition is mainly associated with metabolic syndrome and type 2 diabetes, but also occurs in certain physiological conditions, such as pregnancy or starvation (4). Insulin resistance manifests itself as a wide range of clinical conditions that gradually develop from hyperinsulinaemia

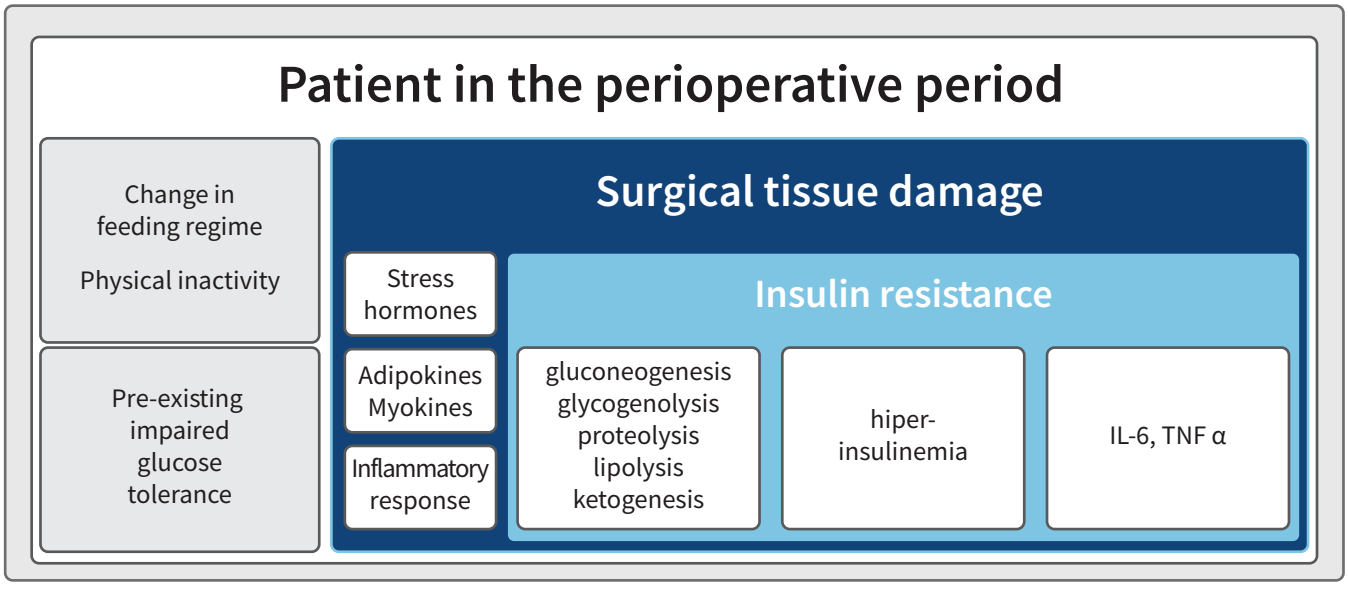

Figure 1: Graphical summary of the background, causes and consequences of insulin resistance in the perioperative period.
Legend: TNF α – tumour necrosis factor alpha; IL-6 – interleukin 6.

to impaired glucose tolerance and eventually to hyperglycaemia, when normoglycaemia can no longer be maintained despite increased insulin secretion. Insulin signalling pathways are disrupted and lipid peroxidation and free fatty acid supply are accelerated. The metabolic consequences of hyperinsulinaemia – glucotoxicity and lipotoxicity – work in synergy to maintain pathological insulin resistance (4,6). Insulin resistance is an inflammatory condition in which atherosclerosis accelerates and endothelial dysfunction develops. It is characterized by overexpression of inflammatory cytokines – tumour necrosis factor alpha (TNFα), adipokines, interleukin-6 (IL-6), C-reactive protein (CRP) – and a decrease in adiponectin (1,4,6).

Transient insulin resistance may also develop with surgical or non-surgical injury or critical illness (3-5). Among the mechanisms described are mainly increased secretion of pituitary gland hormones and activation of the sympathetic nervous system (5). Changes in skeletal muscle, liver and adipose tissue are conditioned by the action of stress hormones and inflammatory cytokines.

Perioperative insulin resistance is predominantly an extrahepatic phenomenon because it primarily affects the skeletal muscle. It is characterized by decreased peripheral glucose uptake and increased endogenous glucose production in the muscle. Insulin facilitates the entry of glucose into insulin-sensitive tissues, e.g. into muscle and adipose tissue, by increasing the number of GLUT-4 transporters. These receptors are stored in intracellular vesicles, so insulin-mediated activation of phosphoinositol-3-kinase causes vesicles to fuse with the cell membrane, resulting in insertion of a transporter into the cell membrane, greater uptake of glucose into the cell and subsequent glycogen synthesis in skeletal muscle. Elevated levels of free fatty acids and inflammatory cytokines (e.g. TNFα) prevent the construction and translocation of GLUT-4 (1,4-6). In the skeletal muscles a subpopulation of GLUT-4 transporters, that increase glucose uptake during exercise, independent of insulin is present as well. Therefore, immobilization results in poorer glucose uptake (5). At the same time, inactive muscle cells secrete less anti-inflammatory myokines, peptides that are otherwise released by muscle cells during exercise. They are active in glucose homeostasis, mainly counteracting proinflammatory adipokines (10).

Metabolic processes in the liver are regulated via endocrine system. The sympathetic system stimulates hepatic gluconeogenesis, while insulin stimulates glycolysis and lipogenesis but inhibits gluconeogenesis. During prolonged fasting, hepatic gluconeogenesis is a major source of endogenous glucose formation. Fasting also promotes lipolysis in adipose tissue and the formation of ketone bodies in the liver (4,5).

Changes in normal metabolic patterns during the perioperative period trigger gluconeogenesis, glycogenolysis, proteolysis, lipolysis, and ketogenesis, which can lead to hyperglycaemia and ketosis, as shown in Figure 1 (1,5,7).

3 Impact of insulin resistance and hyperglycaemia on the outcomes in cardiovascular surgery

The explanations of the effects of hyperglycaemia on morbidity and mortality are complex. In addition, it is not fully understood whether the occurrence of perioperative complications is significantly affected by the mere presence of diabetes or the degree of hyperglycaemia, or whether the presence of insulin resistance itself is more important (7,9,11).

3.1 Insulin resistance in the perioperative period

In one of the few studies conducted by Sato et al., the gold standard technique (hyperinsulinaemic normoglycaemic clamp) was used to document insulin sensitivity during heart surgery in both diabetics and patients without known diabetes. The incidence of major (mortality, acute myocardial infarction, stroke, acute renal failure and infection – sepsis, pneumonia, deep chest infection) and minor post-procedure complications and the duration of hospital treatment was documented. By reducing insulin sensitivity, the incidence of major complications increases significantly, regardless of whether the patient has diabetes or not. In diabetic patients, a negative correlation ($r = -0.527$; $P < 0.001$) was observed between glycated haemoglobin (HbA1c) and insulin sensitivity during surgery. Patients with poorly controlled diabetes had statistically significantly more frequent major complications and infections. They received more blood products and spent more time in the intensive care unit and in the hospital than patients with better glycaemic control (9).

3.2 Preoperative hyperglycaemia – long-term glycemic control

Glycated haemoglobin HbA1c is a measure of glycaemic control regardless of the presence of diabetes. Elevated HbA1c is an independent risk factor for the development of coronary heart disease and stroke (13,14). Data from the literature shows that in candidates for coronary artery bypass grafting (CABG) with known diabetes, HbA1c is 25–50% above target values (15,16). There is also a large proportion of people with undiagnosed diabetes in the general population. It is therefore not surprising that at least 10% of patients have untreated diabetes before cardiovascular surgery (17).

Research on the significance of HbA1c in postoperative outcomes has drawn different conclusions. There is a growing body of literature proving that long-term blood glucose control before surgery affects the short-term outcomes of patients after cardiovascular surgery. HbA1c is an independent predictor of short-term mortality in patients after coronary artery bypass grafting (18). High baseline HbA1c in patients undergoing cardiac surgery predicts an increased likelihood of myocardial infarction, infections, acute renal failure, increased blood product consumption, and longer hospitalization time at surgery. Several respiratory complications and sternal dehiscence have been described (16,18). A review article on the role of HbA1c in predicting morbidity and death after CABG examined 11 studies published up to 2013 that included both surgical patients with diabetes and non-diabetic patients, as well as mixed cohorts (8). Most of the studies included in the article demonstrate a predictive HbA1c value for long-term outcomes. Interestingly, some of the included studies did not prove differences in morbidity and mortality with respect to HbA1c levels, which is most likely due to the design of each study and the set HbA1c limit. The work of Robich et al. (19) is one of the recently published studies which precisely defined the regulation of glycaemia before surgery and adjusted the results taking into consideration other influences. It included more than 6,000 patients after coronary artery bypass grafting and used preoperative HbA1c to predict short-term and long-term CABG survival. Four groups of patients and their risk based on the proportion of HbA1c were identified: subjects with HbA1c less than 5.7%, 5.7–6.4%, 6.5–8.0% and those with HbA1c above 8%. Higher HbA1c values were not associated with higher hospital mortality or morbidity, while long-term survival was significantly poorer in patients with higher HbA1c levels. The risk of death increased by 13% for each increase in HbA1c by one percentage point (adjusted risk ratio, 1.13; $p < 0.001$). The results of this study clearly show that prior glycaemic control assessed by HbA1c predicts long-term survival, and higher levels are associated with poorer outcomes (19).

The risk of both short-term and long-term complications is therefore higher for patients with previously poorly controlled diabetes, but according to the available evidence, there are not enough unambiguous answers for surgery of patients in this category to be postponed until they reached HbA1c targets (16). HbA1c values above 8.6% are associated with up to four times higher risk of death after CABG (8), which proves that improving glycaemic control before surgery could improve surgery outcomes. However, drawing definitive

conclusions is difficult because there are significant differences between studies depending on the observation period, the population of patients involved, and the baseline treatments for diabetes. Above all, post-intervention care may lead to changes in diabetes management relative to baseline HbA1c levels in order to improve glucose control, which may subsequently affect long-term survival.

4 Glucose management before, during and after surgery

Hyperglycaemia, hypoglycaemia, and glycaemic variability have been shown to be detrimental (1), so close monitoring of glycemia is essential. The protocols used to achieve the desired serum glucose targets need to be individualized and adapted to the facility where they are being implemented (1,20).

Most oral glycaemic control medications should be discontinued before surgery. Metformin treatment is discontinued before surgery due to possible deterioration of renal filtration rate, which may occur during surgery (e.g. reduced renal perfusion with haemodynamic instability or dehydration during periods of starvation), which increases the risk of metformin-induced lactic acidosis (21). Insulin secretagogues, namely sulphonylureas (glibenclamide, glimepiride and glipizide), stimulate insulin secretion and may trigger hypoglycaemia in a fasting patient (22). Glucagon-like peptide-1 receptor agonists (GLP-1) (exenatide, liraglutide, dulaglutide, semaglutide) are discontinued on the day of surgery (or the week before) as they slow gastric motility and may slow gastrointestinal recovery. Dipeptidyl peptidase-4 (DPP-4) inhibitors (sitagliptin, linagliptin) act through a glucose-dependent mechanism, so treatment with these drugs can in principle be continued; however, as they lower postprandial glycaemic levels, their effects in the fasting state will not be significant. Sodium-glucose cotransporter-2 (SGLT-2) inhibitors cannot be recommended for routine hospital use until the safety and efficacy of these drugs have been demonstrated. The FDA warns of possible euglycaemic diabetic ketoacidosis using SGLT-2 inhibitors. Therefore, use is discontinued during acute illness when ketone bodies are present, and during prolonged fasting and surgery. Insulin therapy is recommended for the treatment of persistent hyperglycaemia above 10.0 mmol/L, even in patients who have been previously treated with oral antihyperglycaemic agents (1,22).

Long-acting insulin (glargine, detemir) or ultra-long-acting insulin (degludec) can be given to the patient even on the day before the scheduled operation. However, it is advisable to lower the dose by approx. 20% so as not to cause nocturnal or morning hypoglycaemia. Short-acting insulin analogues have a shorter duration of action than human insulins, but in order to prevent the accumulation of insulin when administered subcutaneously in fasting conditions, we switch to intravenous administration (20). In insulin-treated patients, frequent glucose measurements are required to maintain glycaemia in the target area. In addition, serum glucose levels should be monitored every four–six hours in each fasting patient and high levels corected with additional insulin doses (23). Lower insulin requirements are expected in individuals with impaired renal filtration rate or those over 70 years of age. In individuals with a BMI above 35 kg/m2 or a total daily dose of insulin above 80 units (in a patient's home regiment) or following the introduction of a corticosteroid, a high insulin requirement is expected during hospital treatment (1).

Patients with type 1 diabetes require insulin substitution (0.2–0.3 units/kg/day) before and during surgery (23). Stress due to surgical procedure increases the likelihood of diabetic ketoacidosis. The dose of basal insulin should be reduced to 80% in the evening before the scheduled procedure to prevent morning hypoglycaemia. The same principle applies to patients with type 1 diabetes treated with an insulin pump (continuous subcutaneous insulin infusion (CSII or insulin pump therapy)), who could in principle continue with insulin pump use during surgery. If the infusion set of the insulin pump (and sensor system) causes interference due to the proximity of the area of surgery, the anaesthesiologist may switch to intravenous insulin delivery at the same hourly delivery rate as the patient otherwise uses (1).

In most cases, insulin is the most appropriate drug to treat hyperglycaemia in the hospital (1,23). However, it is possible to continue treatment with preoperative regiments, including oral antihyperglycaemic agents, in certain clinical circumstances. Clinical judgment combined with continuous assessment of the patient's clinical condition and blood glucose fluctuations, disease severity, nutritional status, or newly introduced drugs that may affect glucose levels (e.g. glucocorticoids), oral therapy may be reintroduced after surgery (20), if no contraindications have occurred. The decision is individual. Oral treatment should be initiated at least 1–2 days before the planned discharge, which allows for timely consultation with a diabetologist and possible optimization of diabetes treatment before discharge.

Consultation with a diabetologist is recommended especially in case of poor control of glycaemia before surgery, which is indicated by the high HbA1c.

4.1 Critically ill patients with diabetes

In an intensive care and therapy setting, continuous intravenous insulin infusion has been shown to be the best method to achieve glycaemic targets. Intravenous insulin infusions should be dosed on the basis of frequent (hourly) blood glucose measurements that allow infusion rate adjustments to be made taking into account the patient's condition, glycaemic fluctuations, and total daily insulin dose.The use of sliding scale insulin administration is strongly discouraged (20,24).

4.2 Non-critically ill people with diabetes

The basal-bolus insulin dosing regimen (as prandial and correction doses) is the most appropriate treatment for patients who have unpredictable food intake or prolonged starvation. If the patient is eating by himself, doses of short-acting insulin should be adjusted and administered with meals. In such cases, a pre-meal glucose measurement should be performed. When calculating doses, the total daily dose of insulin at the time of infusion may be helpful, which is divided into the basal dose and bolus doses, and the previous doses of the patient if insulin therapy has been initiated prior to hospital treatment. When switching from intravenous insulin infusion to basal subcutaneous insulin infusion, it is safer to discontinue the infusion two hours after administering the long-acting insulin (1). If oral intake is poor, it is safer to dose short-acting insulin immediately after a meal based on the amount of food consumed. If the patient is fed a continuous parenteral diet, this should be followed by a continuous intravenous infusion of insulin. Premixed insulins are not recommended for routine hospital use due to the possibility of more frequent hypoglycaemia (1,20).

5 Perioperative glycaemic targets

Despite the agreement that severe perioperative hyperglycaemia should be corrected, optimal target serum glucose levels that reduce both perioperative complications and the possibility of hypoglycaemia have not yet been established (25). A groundbreaking study conducted by van der Berghe et al. (26) in 2001 recommended strict glycaemic targets for perioperative diabetes control. This was followed by several randomized clinical trials, with different cohorts of patients, that supported intensive perioperative glucose control (27). In 2004, however, Lazar et al. demonstrated that maintaining serum glucose levels between 6.7 – 10 mmol/L during cardiovascular surgery is safer, and a stricter regimen does not contribute to improved outcomes (28). However, the optimal target range for blood glucose levels in critically ill patients remains unclear for the time being. An international randomized NICE-SUGAR study involving more than 6,000 patients found that intensive monitoring of serum glucose levels increased mortality in intensive care units. Less stringent targets for serum glucose (below 10.0 mmol/L) resulted in lower mortality than stringent targets (4.5–6.0 mmol/L); the risk ratio was 1.14; $p = 0.02$. In the intensive care group, hypoglycaemia was reported in 6.8% of patients compared with 0.5% in the control group. There were no differences between the groups in the duration of mechanical respiration, the duration of treatment in the intensive care unit, or the total duration of hospitalisation (11). A study by Desai et al. found that maintaining serum glucose levels after CABG in the liberal range led to similar outcomes compared to the strict glucose target range (29).

The Society of Thoracic Surgeons (STS) recommends a blood glucose level target range of 6.7–10 mmol/L for CABG patients and maintenance of serum glucose levels ≤ 10 mmol/L for at least 24 hours after heart surgery (30). The Society for Ambulatory Anaesthesia (SAMBA) recommends intraoperative blood glucose levels <10 mmol/L (31). The American Association of Clinical Endocrinologists (AACE) and the American Diabetes Association (ADA) recommend a glucose level target between 7.7–10 mmol/L in critically ill individuals (32). Recent ADA guidelines recommend a glucose level target range of 7.8–10.0 mmol/L for most critically ill patients (20). Stricter targets, < 7.8 mmol/L, are also appropriate for selected patients if this can be achieved without a significant risk of hypoglycaemia. In contrast, higher glucose levels may be acceptable in acutely ill patients with poor outcome prognosis, in patients with advanced co-morbidities, and in hospital settings where frequent monitoring of serum glucose levels or close monitoring is not feasible (20). In palliative care, the main goal of treatment is to prevent possible hypoglycaemia and a prolonged rise in glycaemia above the glucosuria threshold, i.e., above 15 mmol/L, which causes symptoms. With such a palliative approach, we strive to improve the quality of life and not to prevent chronic complications (23).

6 Comprehensive treatment of a patient with diabetes in cardiovascular surgery

Large randomized trials weighing the advantages of surgical and percutaneous coronary interventions over optimal drug treatment have identified subgroups of patients who benefit more from surgical revascularization (33). These are patients with multivessel coronary artery disease and left main coronary artery disease, left ventricular dysfunction or diabetes (34). When deciding on the most effective therapeutic approach in diabetic patients, we are guided by key variables: the extent and anatomy of coronary artery disease (assessed with the SYNTAX rating scale), surgical risk, EuroSCORE II or STS score, and the surgeon's experience. However, these patients are diverse in terms of the risks and benefits associated with coronary artery bypass grafting. Optimal drug treatment remains the cornerstone of cardiovascular disease treatment in patients with type 2 diabetes, either as a primary or secondary prevention (34). The inclusion of clinical characteristics of the patient in an established anatomical assessment of the severity of CVD may offer a more reliable risk assessment for patients with complex multivessel coronary artery disease (36). This is especially true for the population at high-risk for cardiovascular disease, which includes all diabetic patients. International guidelines dictate the need for a local multidisciplinary team consisting of a non-invasive cardiologist, an interventional cardiologist, and a cardiac surgeon to decide on the best treatment for the patient. Late complications in patients who initially survive CABG are less affected by traditional early mortality calculations (such as EuroSCORE). Long-term survival is increasingly associated with the possible presence of chronic diseases such as diabetes, because diabetes is a systemic disease with diffuse atherosclerotic effects on coronary arteries. The vessel diameter is significantly smaller and the atherosclerotic plaque longer, which affects not only the revascularization strategy, but also the lifespan of the graft (37).

According to several studies, the effect of intensive glycaemic control on macrovascular complications is less convincing than the effect on microvascular complications (38). Therefore, a glucocentric approach to diabetic patient treatment is being replaced by an emphasis on antihyperglycemic drug class selection. Different classes of drugs for the treatment of hyperglycaemia are associated with different effects on cardiovascular risk. Insulin and sulphonylureas are risk-neutral for CVD, and their significant side effects include weight gain and hypoglycaemia (39). SGLT-2 inhibitors are the first drugs for which clear benefits for cardiovascular risk have been demonstrated (40). Some of the GLP-1 agonists have also been shown to reduce the incidence of major adverse cardiovascular events (MACE) (39).

6.1 Proactive approach to insulin resistance in cardiac surgery - ERAS, enhanced recovery after surgery

Enhanced Recovery After Surgery (ERAS) is a multidisciplinary initiative to improve care throughout the perioperative period. In the 1990s, ERAS was introduced by a group of surgeons in a desire to improve the perioperative care of their patients. From the field of abdominal surgery, the principle has moved to all areas, including cardiac surgery (41). ERAS is based on evidence-based perioperative care protocols which can lead to improved clinical outcomes, reduced complications, and reduced costs also due to a significant shortening of hospitalization and earlier return to normal life (42). ERAS is also used in Slovenia as a model of perioperative treatment, in which we optimize patient's recovery by optimizing treatment processes (43,44).

ERAS in cardiac surgery or CARDIAC ERAS

The ERAS-Cardiac guidelines are based on the available evidence in cardiac surgery. The applicability of ERAS principles in vascular surgery is limited, and there are no targeted guidelines for their use in vascular surgery because the existing evidence in the literature is insufficient and of low quality. While rare publications describe the use of ERAS pathways in thoracic and abdominal aortic surgeries, descriptions of ERAS pathways in peripheral arterial system surgeries are insufficient. Such descriptions do not yet exist in endovascular surgery (45). The implementation of ERAS pathways in the care of patients after complex operations on the thoracic and abdominal aorta (can be performed with or without the use of extracorporeal blood circulation) is more applicable to cardiac surgery (i.e. ERAS-Cardiac).

6.1.1 Assessment of haemoglobin A1c for risk assessment according to cardiac ERAS principles

Based on evidence suggesting a predictive HbA1c value for outcomes after major surgeries, the ERAS-Cardiac guidelines recommend HbA1c measurements to help assess preoperative risk. The guidelines call for a preoperative examination of all diabetics and the

introduction of measures to improve glycaemic control to achieve HbA1c levels below 7% (41).

6.1.2 The fasted state before surgery

Some research suggests that consumption of a complex carbohydrate rich drink (e.g. up to two hours before surgery) may reduce post-surgery insulin resistance (46). This avoids the starvation-related catabolic process. An improvement in insulin sensitivity is expected, and thus a lower risk of postoperative hyperglycaemia (47). Encouraging the consumption of clear fluids two to four hours before surgery is an important component of all ERAS protocols (41). However, a meta-analysis did not show a reduction in complications or a shortening of the duration of hospitalization when patients who consumed carbohydrate preparations before surgery were compared with those who received placebo (48). No major studies in this area of preoperative care have been performed in the field of cardiovascular surgery. A small study conducted by Breuer et al. found that an oral carbohydrate drink consumed two hours before surgery was safe and that there were no complications during nor after surgery. In patients who underwent surgery using extracorporeal circulation, the use of the ERAS-Cardiac protocol showed a reduced need for inotropic support during surgery (49).

6.1.3 Insulin infusion

The ERAS-Cardiac guidelines advise hyperglycaemia treatment up to the glucose level target of 8.8–10 mmol/L by insulin infusion, with the aim of preventing post-operative hypoglycaemia. Due to the lack of clinical research in the field of cardiovascular surgery, the level of recommendation was IIa (41).

6.1.4 Choice of anaesthesia

General anaesthesia is more commonly associated with hyperglycaemia and higher concentrations of catecholamines, cortisol, and glucagon than local or epidural anaesthesia. Volatile anaesthetics inhibit insulin secretion and increase hepatic glucose production (1,41).

6.1.5 Effectiveness and implementation of ERAS principles in cardiac surgery

Initial results of ERAS-Cardiac studies involving cardiovascular surgical patients showed similar benefits as in other surgical patients, including improved perioperative pain control (25–60% reduction in opioid use), improved early rehabilitation, and a faster transition to oral nutrition, shortening of care in intensive care units (by four to twenty hours) and shortening of the duration of total hospitalization (by one to four days). Evidence that adherence to the ERAS protocol in cardiovascular surgical patients is expected to reduce the incidence of perioperative atrial fibrillation by 8–14% is also clinically relevant (50).

7 Conclusion

There is ample evidence that perioperative insulin resistance, which occurs in as many as 80% of patients in the field of cardiovascular surgery, has a significant effect on the occurrence of short- and long-term complications and on mortality after cardiovascular surgery. Although treatment of patients with perioperative hyperglycaemia is always individualized, it has been recognized to date that following perioperative patient treatment protocols (e.g. ERAS), which are the result of multidisciplinary approaches and include all cardiovascular surgical patients, leads to improved surgical treatment outcomes in individuals. Therefore, it would be sensible and necessary for clinical perioperative treatment of cardiovascular surgical patients to be uniformly adapted to the latest findings and new multidisciplinary protocols (Figure 2).

Conflict of interest

None declared.

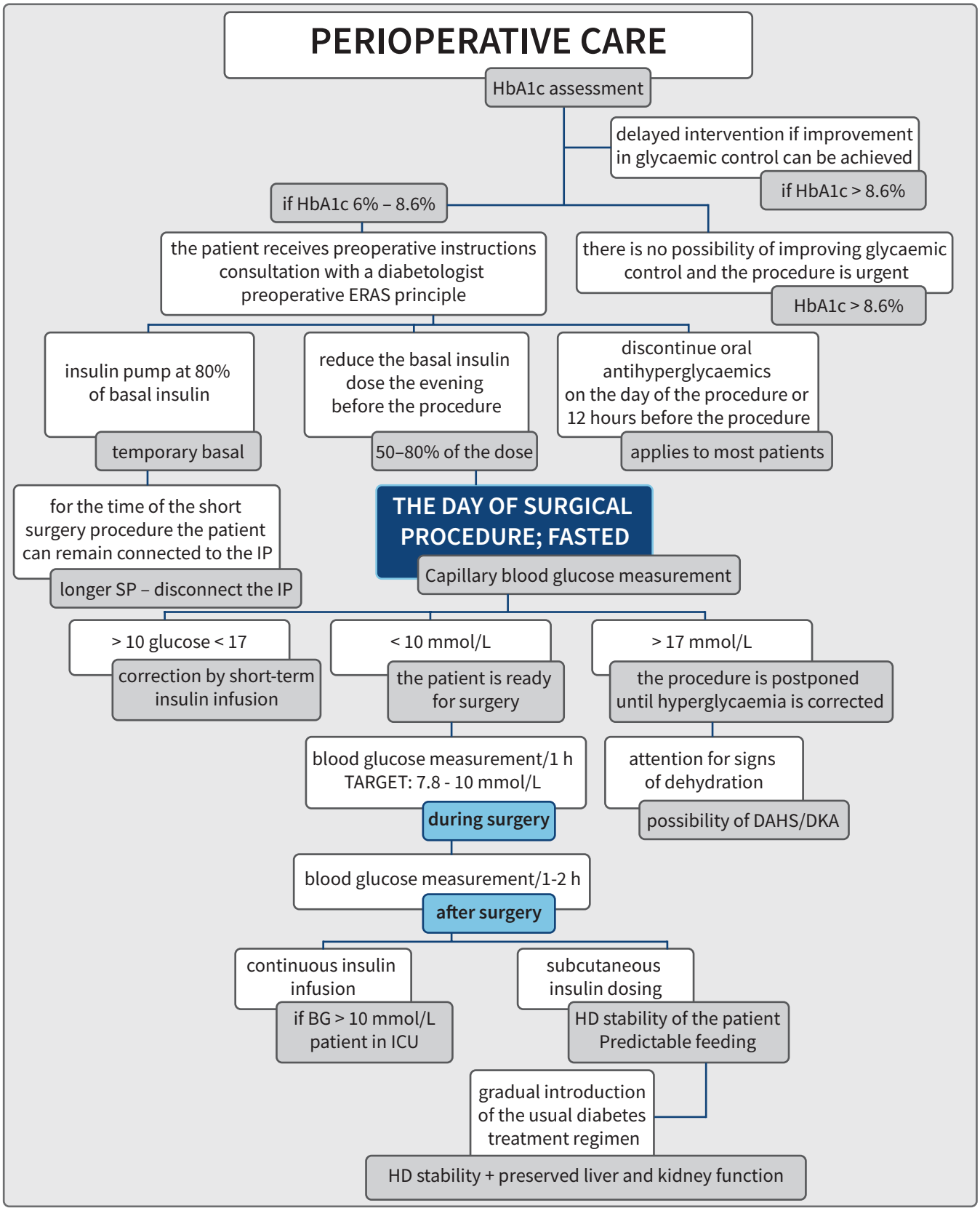

Figure 2: Algorithm of action in preoperative and intraoperative treatment of patients with or without known diabetes in the planning and course of the procedure in cardiovascular surgery. Adapted from (1,8,22–24,41).

Legend: BG – blood glucose; D2 – type 2 diabetes; D1 – type 1 diabetes; ICU – intensive care unit; IP – insulin pump: Continuous subcutaneous insulin infusion (CSII or insulin pump therapy); CH – carbohydrates; ERAS – Enhanced Recovery After Surgery; HbA1c – glycosylated haemoglobin.

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