Clinical benefits of tight glycaemic control: Focus on the perioperative setting

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The benefits of tight glycaemic control (TGC) were first shown in cardiac surgical patients with diabetes. These concepts migrated to other surgical and medical specialties through intensive care units caring for a variety of patients with a variety of disease states. Although some disagreement and controversy surrounds the use of TGC in the medical population, the benefits of this therapy in the diabetes cardiac surgery population is unblemished. Perioperative hyperglycaemia has been shown to be associated with adverse surgical outcomes in several different patient populations. TGC for 3 full postoperative days or more mitigates these risks. Although this has been definitively proven in the diabetes coronary artery bypass graft (CABG) population, evidence for beneficial effects of TGC in other surgical populations remains elusive at this point in time. In this article, we explore the risks of hyper- and hypoglycaemia in the surgical patient; safety and efficacy of insulin protocols in the surgical population, target range goals and duration of therapy; the beneficial effects of TGC on decreasing mortality, reducing infectious complications, length of stay and other complications; define target surgical populations that benefit from TGC; analyse current controversies as they relate to surgical populations; and describe questions that remain for the future of TGC.

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Although there has been much controversy1–3 surrounding the use of tight glycaemic control (TGC) as a panacea for all hospitalised patients, the wide-ranging benefits of insulin infusions in the surgical patient during the perioperative period has been much less prone to debate. In fact, perioperative TGC

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in the cardiac surgical patient with diabetes is, at this point in time, incontrovertible and is considered by most adjudicating bodies a standard of care.4 Indeed, the entire concept of in-hospital glycaemic control first came to light through the groundbreaking studies done on the diabetic cardiac surgery population in Portland in the early 1990s.5–7 These were followed by the landmark surgical intensive care study from Leuven, in which there was a heavy preponderance of cardiac surgery patients.9 No study to date has disproven the beneficial effects of perioperative TGC in the diabetic cardiac surgery population, although insightful questions remain about the timing, duration, target range and the actual target population of such control.4

In this article, we review the current thinking about the state of the art of TGC in the perioperative setting with a special focus on the cardiac surgery patient. We explore the published detrimental effects of hyperglycaemia and hypoglycaemia in the surgical population, the application of insulin and glucose–insulin–potassium infusion (GIK) protocols to the surgical patient – preoperatively, in the operating room, in the Intensive care unit (ICU) and on the non-ICU ward; results of TGC and glycaemic studies on mortality, infection and length of stay (LOS); optimal target range and duration for TGC therapy, proven and presumed target populations for TGC; and review the few countervailing studies that purport to weigh in against the benefits of TGC in the surgical population.

Hyperglycaemia (is bad)

The Portland Diabetes Project, which began in 1992 in Portland, OR, USA, was the first prospective study to elucidate the clinical connection between perioperative hyperglycaemia and increased perioperative morbidity (infection rates)5 and mortality.7 That continuing body of work now encompasses over 6500 cardiac surgery patients with diabetes. This group has shown that hyperglycaemia >10 mmol is independently associated with a threefold increase in deep sternal wound infections (mediastinitis). In addition, this large study cohort has taught us that mortality, LOS and number of overall complications in the diabetic coronary bypass (CABG) population show significant and steady increases as average glucose levels rise above 8.3 mmol.9 Other studies have confirmed that uncontrolled hyperglycaemia in hospitalised CABG patients increases their risk of infection,10–12 myocardial damage13 and death.10,12

McAlister et al.14 revealed a significant association between the average glucose levels on the first postoperative day following CABG and increased overall adverse outcomes, notably stroke. It is widely accepted that extreme hyperglycaemia is detrimental to outcomes. Fish and co-workers15 showed that blood glucose (BG) levels >14.4 mmol in CABG patients are associated with a 10-fold increase in complications, while our group has shown a 14-fold increase in CABG mortality at similar BG levels. In a large retrospective review of all cardiac surgery patients, Doenst found that increasing BG levels during surgery were found to be an independent predictor of in-hospital mortality in all patients regardless of their diabetes status.16 Finally, elevated preoperative fasting glucose levels were shown to predict a 50% reduction in survival at 1 year17 as compared with those with normal fasting BG levels.

In addition to cardiac surgery, hyperglycaemia is associated with poor outcomes in orthopaedic surgery, peripheral vascular surgery, colorectal surgery, urologic surgery, burn surgery18 and trauma surgery.19,20 Using the United States Nationwide Inpatient Sample, Marchant and co-workers21 retrospectively reviewed over one million cases of total joint arthroplasty and correlated their outcomes with the level of pre- and perioperative glycaemic control as assessed by BG levels, the haemoglobin A1c level and diabetes–related co-morbidities. They showed that poor glycaemic control resulted in increased rates of death, wound infections, stroke, LOS and other complications. Thus, as compared to both non-diabetic and controlled diabetes patient controls, uncontrolled diabetes mellitus exhibited significantly increased odds of surgical and systemic complications, higher mortality, and increased length of stay during the index hospitalisation following lower extremity total joint arthroplasty. In the vascular surgery world, poor perioperative glycaemic control was associated with unfavourable outcomes – death, major amputation or graft occlusion at 90 days – after infragenual bypass surgery in diabetic patients.22 In trauma patients, Collier found a two- to threefold increase in death in those who experienced 1 or more days of BG levels >8.3 mmol.19
Finally, in a large retrospective study of 259,000 patients from the US Veterans Administration Hospitals, hyperglycaemia was shown to have a significant relationship with severity-adjusted mortality rates in several differing surgical populations, including those undergoing CABG and valve surgery, colectomy, resection of genito-urinary neoplasms and peripheral vascular bypass surgery. Taken together, these studies and others provide ample evidence that hyperglycaemia increases morbidity and mortality not only in the cardiac surgery patient population, but in other surgical populations as well.

Hypoglycaemia (is bad)

TGC is a double-edged sword, as severe hypoglycaemia can also be detrimental to clinical outcomes. This long-known and clinically palpable medical fact evokes special concern in TGC trials as the detrimental effects of hypoglycaemia can work against the beneficial effects of hyperglycaemic control. This was first seen in the Leuven MICU study in which regression analysis revealed an independent relationship between a single hypoglycaemic episode and death. Krinsley then showed that in a mixed ICU setting a single episode of severe hypoglycaemia (<2.2 mmol) independently increased the risk-adjusted rates of in-hospital death more than 2 times. Bagshaw et al. have now confirmed these findings in a study of 66,184 patients. They showed that a single episode of hypoglycaemia <2.2 mmol increases the risk-adjusted mortality by 2.6 times. Although the countervailing detrimental effects of hypoglycaemia during TGC have been demonstrated only in non-surgical studies, these lessons must be applied to surgical protocols and treatment groups to maintain overall safety.

Insulin protocols – safety and efficacy

A number of insulin protocols have been published for use in the intra-operative and postoperative ICU and postoperative non-ICU settings. The dual goals of all these protocols are to rapidly achieve and maintain a specified target BG range – known as ‘efficacy’ – while still avoiding the occurrence of hypoglycaemia – known as ‘safety’. Intravenous insulin delivery is the preferred method for controlling BG levels in the surgical patient, both in the operating room and in the postoperative ICU. The direct intravenous route of delivery allows for immediate delivery of insulin to the cellular level, rapid titration to target BG range and thus efficacious BG control even in the face of insulin resistance, endogenous insulin depletion and subcutaneously malabsorbive states (during periods of decreased cutaneous blood flow such as when patients are hypotensive or on pressors) – as often occurs in the intra- and postoperative state. CABG surgery patients, in particular, benefit from direct delivery to the myocardial mitochondria with a demonstrable shift of myocardial metabolism away from the free fatty acid (FFA) cycle to the aerobic glycolysis pathway. This is one of the main proposed mechanistic pathways for the decrease in cardiac-related mortality in the diabetes CABG population treated with insulin infusions.

Because of this ability to metabolically shift the myocardial energy sources, glucose–insulin–potassium (GIK) drips have been used in cardiac surgery patients in an attempt to metabolically manipulate the heart and force a conversion away from FFA utilisation to aerobic glycolysis, even in the absence of hyperglycaemia. This has never proven to be clinically effective in the non-DM cardiac surgery population, except for patients in cardiogenic shock. Nonetheless, the effective ‘component’ of GIK is believed to be insulin, which is now used instead of GIK.

The efficacy of any protocol can be measured by the time it takes to bring the patient into a specified target range; the percent of time the patients spend in the target BG range; or the actual average BG achieved while on the protocol as compared with the intended target BG. However, safety should be measured by the number of episodes of hypoglycaemia that occur per patient (not per measurement) on any given protocol and the average time the patient spends in a hypoglycaemic state before being corrected to euglycaemia. Hypoglycaemia has been variably defined as any BG reading less than 2.2–4.0 mmol, depending on the study. As an example of safety reporting, current data from the Portland Protocol database reveal that 0.5% (1 out of 200) of all patients on the protocol – with a target of 3.9–6.1 mmol – experience a single episode of hypoglycaemia <2.2 mmol. The average time until the patient is once again >3.9 mmol is 33 min.
More efficacious protocols achieve target ranges faster and hold patients in the range longer, while safer protocols produce less hypoglycaemia. Protocols that target lower BG ranges (e.g., 4.0–6.0 mmol) must be made more complex and require more frequent BG checks than the protocols that target higher ranges (e.g., 8.0–10.0 mmol) to achieve similar efficacy and safety scores.

Clinical benefits of TGC: Mortality reduction

The beneficial effects of TGC in reducing in-hospital surgical mortality have been demonstrated mainly in the cardiac surgery population, and particularly in those with diabetes who are undergoing CABG. The Leuven I study randomised 1548 ventilated patients admitted to the surgical ICU to receive either TGC (4.4–6.1 mmol target) to conventional glycaemic control (10–11.1 mmol target). The study cohort included 970 patients (63%) who were admitted to the ICU immediately after elective cardiac surgery or for subsequent complications resulting from that surgery. TGC was shown to reduce ICU mortality by 43% – (8.0% vs. 4.6%) in this predominantly cardiac surgical population. Hospital mortality for all cardiac surgery patients in this study was significantly reduced from 5.1% to 2.1%.

The first application of TGC in any clinical population occurred in the non-randomised, prospective, observational, Portland Diabetes Project. This was the first trial to use intravenous insulin infusions – starting in 1992 – to routinely control BG in cardiac surgery patients with diabetes. In the CABG subset of patients, insulin infusions were shown to independently reduce risk-adjusted in-hospital mortality by 68% compared with then-conventional subcutaneous insulin (SQI) control. The mortality reduction was primarily due to a reduction in cardiac-related death – arrhythmias and pump failure – 4.1% incidence with SQI versus 1.1% with TGC.

Delasandro and co-workers retrospectively studied 300 diabetes CABG patients receiving TGC and compared their risk-adjusted outcomes to 300 propensity-matched historical CABG controls. They found that mortality was significantly lower than expected in the TGC group (as predicted by EuroScore – 1.4% vs. 4.3%) with a profound mortality reduction (8.0% vs. 2.5%) seen in the higher risk (EuroScore >4) cohort. There is an additional retrospective study of 1050 non-diabetic cardiac surgery patients from Belgium, which showed a 70% decrease in the 30-day mortality in the 745 patients on TGC compared with 305 historical controls who were not given TGC.

Clinical benefits of TGC: Reducing infection

In a meta-analysis by Brown, the presence of diabetes in the cardiac surgery population was shown to confer a threefold increased risk of postoperative wound infection in cardiac surgery patients. This clinically known adverse outcome was directly addressed by the initial work from Portland. These studies first confirmed the association between elevated perioperative BG levels in patients with diabetes and subsequent sternal infections. Postoperative BG levels between 10 and 12 mmol increased the risk of infection 2 times, between 12 and 14 mmol they were increased 4 times and above 14 mmol the rate of infection increased sixfold. Notably, there was no increase in surgical-site infections at BG levels below 10 mmol. The project then went on to prove that the infectious risk previously ascribed to ‘diabetes’ could be totally eliminated by TGC methodology. Insulin infusions independently reduced sternal infection rates by 77% in this diabetes cardiac surgery population – normalising those rates to that of the non-diabetic population.

In a retrospective study of CABG patients with diabetes, Hruska and co-workers found that TGC with a target range of 6.7–8.9 mmol significantly decreased the incidence of sternal infections as compared to SQI controls. This confirms the findings from Portland that indicate the immune-compromising effects of hyperglycaemia begin at 10 mmol. In a similar fashion, Lazar showed a significant reduction in sternal infections with TGC in a prospective randomised cohort of CABG patients. Again, in a predominant, but not purely cardiac surgical population, Van den Berghe’s SICU study found a 46% reduction in the occurrence of sepsis in the TGC group when compared to the conventional control group. Although there are excellent data correlating hyperglycaemia to non-cardiac surgical wound infections, there are no studies confirming that TGC lowers surgical wound infection rates in non-cardiac surgical patients.
In the non-cardiac surgery population, TGC has been associated only with a decrease in infectious complications. Intensive insulin therapy for burn-injured patients admitted to the ICU was associated with a reduced incidence of pneumonia, ventilator-associated pneumonia and urinary tract infection. However, TGC did not result in a change in mortality or LOS when adjusting for confounding variables.18

TGC was evaluated in 1108 patients from the Maryland shock-trauma centre and compared with 1021 immediate historical controls. The incidence of infection significantly decreased from 29% to 21% in the TGC group.20

Clinical benefits of TGC: Decreasing complications and LOS

In a retrospective review of 1050 non-diabetic cardiac surgery patients, 745 of whom were on TGC, Lecomte and co-workers34 showed that TGC was associated with a significantly reduced incidence of both acute kidney injury and renal failure according to the RIFLE (Risk, Injury, and Failure; and Loss, and End-stage Kidney Disease) criteria and reduced the overt incidence of postoperative new-onset dialysis from 3.9% to 0.7%. Using the Cleveland Clinic Renal Severity Score, they confirmed that the incidence of renal failure with TGC was significantly lower than predicted, while in the control group it was as expected.

Reductions in length of hospital stay have been associated with implementation of TGC protocols in surgical populations. The Portland studies have shown that there is a direct correlation between increasing postoperative glucose levels and increasing length of hospital stay. Conversely, LOS is reduced by 1 day for every 4.3-mmol reduction in the 3-day average postoperative BG levels – known as ‘3-BG’ (see below).9 Scaela has also shown decrements in LOS and ventilator days when comparing TCG treated trauma patients with non-TGC controls.20 There are no other studies in the surgical population that examine length of hospital stay with regard to TGC.

Target range

Examination of hyperglycaemia levels as they relate to the three major adverse clinical outcomes in the surgical populations noted above seems to reveal that:

1 – The upward inflection point for an increase in surgical mortality as related to BG is unknown, but is certainly somewhere below 8.3 mmol
2 – The upward inflection point for an increase in surgical wound infection rates as related to BG begins at 10.0 mmol.
3 – The upward inflection point for an increase in surgical LOS as related to BG is unknown, but is somewhere below 8.3 mmol.

Taking these three factors into account, it seems reasonable to conclude that BG levels in the perioperative patient should be maintained at or below 8.3 mmol at all times to optimise postoperative outcomes. TGC protocols that are effective in safely maintaining this type of control, without inducing hypoglycaemia, should be sought out and used especially in the cardiac surgery population.

In the non-cardiac surgery population of patients who are not in the intensive care unit, the primary goal of TGC protocols is to avoid infectious complications. This is because neither mortality nor LOS has been definitively associated with perioperative hyperglycaemia in this population of patients. Therefore, every effort should be made to keep BG less than 10 mmol, but there seems to be no apparent need for the upper target to be lower than this in the non-ICU, non-cardiac surgery population.

However, in the non-cardiac surgical patient who is admitted to the ICU, and may remain there for a prolonged period of time, true TGC – with an upper BG target of <8.3 mmol or lower – should be implemented and maintained until discharge from the SICU.

Duration of therapy – the concept of 3-BG and postoperative TGC

While BG target level considerations have been the subject of much heated debate over the past several years, the concept of duration of therapy has been largely ignored. This is because, outside of
the cardiac surgery world, the concept of TGC is believed to be an ‘ICU-only’ therapy. However, this location-centric concept has been largely ignored by the major cardiac surgery studies of TGC, where the detrimental effects of hyperglycaemia are believed to be time weighted rather than location based.

The Portland studies have shown that the detrimental effects of hyperglycaemia on the above three key outcomes persist for at least 3 days following open-heart surgery in patients with diabetes. There is an independent association of elevated BG levels to the occurrence of mortality, infection and prolonged LOS on the day of surgery, the first postoperative day and the second postoperative day – no matter where the patient is located, or stays, within the hospital walls (Table 1). These associations are statistically significant and appear to be time weighted. By the fourth postoperative day, there appears to be no association between hyperglycaemia and any outcome, as long as the patient has been discharged from the ICU.

Our studies have shown that the majority of hyperglycaemic-mortality risk for the cardiac surgical patient occurs in the first three postoperative days; the majority of the infection risk occurs in the first three postoperative days and the majority of the prolonged LOS risk occurs in the first three postoperative days. For this reason, the Portland group has defined what is now known as 3-BG – or the average 3-day postoperative glucose – as the primary BG metric against which adverse outcomes are gauged. For those same reasons we believe insulin infusions should be used to maintain TGC for at least three postoperative days in all cardiac surgical patients – regardless of where they are located in the hospital. In the Portland study, patients are not kept in the ICU just because they still require insulin infusions to optimise their perioperative outcomes. Therefore, we have employed intravenous insulin infusions even on the non-ICU wards since 1995 in our postoperative cardiac surgery patients who would otherwise be hyperglycaemic. This important ‘duration’ component to TGC therapy is missed if TGC is considered to be an ICU-only therapy. We believe, and our results show, that the duration of therapy is just as important as target BG level ... or as we like to say: The ‘3’ is just as important as the ‘BG’.

However, there does appear to be a location-centric effect beyond the third postoperative day if, and only if, the patient, must remain in the ICU beyond that time for medical reasons. In that case, the association between hyperglycaemia and detrimental outcomes remains in place at least as long as the patient continues to reside in the ICU. This duration effect was also shown in the Leuven I study, where the mortality benefit in this mixed surgical population was confined to those patients who remained in the SICU and on insulin drip for more than 5 days. Further corroborating the concept of duration of therapy are the pooled results from the Leuven I and II studies, which revealed an absolute mortality reduction of 7.8% with TGC (compared with conventional control) in patients who remained in the ICU and on insulin infusion for more than 3 days. In those patients who left the ICU prior to 3 days – and were thus taken off the TGC insulin infusion protocol ‘early’ – there was no significant change in mortality.

**Preoperative Care**

The Portland studies further confirm the link between one postoperative outcome – sternal infection – and preoperative hyperglycaemia (Table 1). There are no other significant associations between preoperative glucose levels and postoperative outcomes as long as insulin infusions achieving TGC are used for three postoperative days. Therefore, the sole preoperative indication for starting an insulin infusion before an operation is a preoperative BG level greater than 10 mmol, as this is the threshold for increased postoperative wound infection rates. In these patients, we recommend starting insulin infusions the night before surgery and we do so on the non-ICU floor, or in the preoperative stay unit.

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<th>Table 1</th>
<th>Independent Significance of daily glucose parameters on Outcomes.</th>
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<td>HgbA-1C</td>
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<td>Mortality</td>
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Glycaemic control in the operating room has again only been studied in the cardiac surgical patient population. Doenst found that higher intra-operative BG levels were predictive of mortality in cardiac surgery patients with and without diabetes. Gandhi also confirmed that hyperglycaemia was related to both mortality and postoperative complications in a retrospective review of 409 cardiac surgical patients.

We have shown that rapid and effective intra-operative glycaemic control is integral to the TGC process and cannot be separated from it. We therefore begin our insulin infusions in any patient who becomes hyperglycaemic in the operating room during cardiac surgery. Because of the need to rapidly establish control in the operating theatre, where cardiopulmonary bypass and core body temperature cooling cause decreased insulin secretion and increased insulin resistance, respectively, we do not follow a written protocol. Rather, our anaesthesiologists have developed methods of rapid control using a combination of frequent (every 15–20 min) intravenous bolus insulin dosing along with rapid titration of insulin infusions. We believe that aggressive intra-operative glycaemic control, along with frequent intra-operative monitoring in the anaesthetised patient is the cornerstone for establishing good TGC in the postoperative period.

**Target populations**

So, what surgical populations should be targeted for TCG therapies? There is a good argument that TGC protocols are safe and effective in improving outcomes in cardiac surgery patients with diabetes. This has been proven without exception by several studies. Studies showing similar improvements in cardiac surgery patients without diabetes are lacking. In fact, data from 13 000 non-diabetic CABG patients from the Portland Project show no significant differences in mortality (2.5% vs. 2.6%) or sternal infection rates (0.35% vs. 0.24%). Nonetheless, there is a high proportion of patients admitted for such surgery who are diagnosed with diabetes during cardiac surgical admission. In addition, no clinically detrimental effect of hypoglycaemia has been reported in any cardiac surgical population on a TGC protocol. Therefore, it is reasonable to treat all cardiac surgery patients who experience hyperglycaemia with TGC protocols to control and eliminate that hyperglycaemia.

In addition, any surgical patient, who is admitted to the ICU, is placed on intravenous total parenteral nutrition and is expected to, or may possibly remain in the ICU for more than five postoperative days, should be started on an insulin protocol for TGC. Because LOS in the SICU cannot be definitively predicted, it is safe to say that all post-surgical ICU patients should be started on TGC protocols, as it is the first few days of glycaemic control that seem to matter the most in terms of improving outcomes (Table 1).

There is fledgling evidence, albeit less convincing than the diabetes–cardiac surgical population, that surgical patients admitted to trauma units and burn units may indeed benefit from TGC protocols.

Outside of the cardiac surgery, burn and trauma patient populations, there is little direct evidence to support the use of TGC protocols to improve outcomes in other surgical patients. Although hyperglycaemia on admission in several studies appears to correlate with a worse outcome, early glucose normalisation with TGC protocols has not been shown to affect morbidity and mortality in several critically ill surgical populations. Nonetheless, there is emerging evidence that other surgical patient populations may eventually be shown to benefit from TGC. These potential future surgical TGC populations may include orthopaedic, colorectal, genito-urinary neoplasm and peripheral vascular surgery patients.

**Countervailing studies – the ‘naysayers’**

There are several studies that argue against the use of TGC protocols, even in the cardiac surgery population. One such study by Gandhi attempted to randomise only the intra-operative component of TGC therapy in cardiac surgery patients. Although no differences were found in the outcomes, this study of less than 400 patients was extremely underpowered to definitively answer such a hair-splitting question.

Finally, the widely publicised NICE-SUGAR study of 6100 ICU patients from 42 centres in Australia, New Zealand and Canada claimed a detrimental effect of TGC on 90-day mortality in the overall patient
cohort, in which one-third of the patients were identified as post-surgical. Clinicians should note that the results of NICE-SUGAR do **NOT** apply to the cardiac surgical population, as few, if any, such patients were enrolled. The authors have yet to perform a subgroup analysis on the remaining non-cardiac surgical population and evaluate the potential effect of TGC and induced hypoglycaemia on the 90-day mortality. Until those analyses occur, and are openly vetted on the peer-reviewed stage, TGC should continue to be used in SICU populations noted above.

Questions/Endorsements/Conclusions

Many questions still remain to be answered and divergent theories need to be unified in the field of TGC. What populations benefit, other than CABG patients with diabetes, trauma, burn and long-term SICU patients on TPN? What is the optimal duration of TGC therapy? Does TGC improve outcomes in non-diabetic cardiac surgical patients? Should TGC only be applied in the ICU, or are outcomes enhanced with extended use on the non-ICU ward as was seen in the Portland studies? Does TGC improve outcomes in other surgical populations whose outcomes seem to be negatively affected by hyperglycaemia?

Despite these lingering questions, TGC has proven to be a life-saving, complication-reducing, cost-saving therapy in cardiac surgery, trauma, burn and long-term surgical ICU patients. As such, glycaemic control protocols have been endorsed for postoperative patients by the Society of Thoracic Surgeons, the US Centers for Medicare and Medicaid Surgical Care Improvement Project, the American Association of Clinical Endocrinologists, the American Diabetes Association and the United States National Quality Forum. Insulin infusions are the cornerstone of TGC management in the surgical patient population.

Practice points:

- 3-BG – the 3-day average blood glucose level – is the key metric related to adverse outcomes in surgical patients
- BG threshold for infectious complications begins at 10 mmol
- BG threshold for increased mortality, LOS and other complications begins below 8.3 mmol
- Target range for TGC should always maintain BG levels below 8.3 mmol for optimal clinical results, while avoiding hypoglycaemia
- Duration of TGC therapy is as important as BG target range in achieving optimal clinical results with TGC protocols
- TGC should not be limited to use in the ICU
- Results from the NICE-SUGAR study do not apply to the cardiac surgery population

Research agenda:

- How does glycaemic variability affect outcomes in the cardiac surgical population?
- Does TGC improve outcomes in the non-diabetic CABG population?
- Does TGC improve mortality and decrease complications in the vascular surgery/colorectal surgery/GU neoplasm surgery and orthopaedic surgery populations?
- Does the concept of 3-BG – including hyperglycaemia outside of the ICU, but within 3 days of surgery – apply to infectious complications in non-cardiac surgical patient populations?
- Does perioperative hypoglycaemia affect surgical mortality? If so, at what level and at what duration?
- Will continuous glucose monitoring improve the safety and efficacy of TGC insulin protocols?
- Are basal-prandial subcutaneous insulin protocols outside of the ICU as effective as insulin infusions in controlling hyperglycaemia and optimising outcomes in the cardiac surgical population?
References


