An-Najah National University

Faculty of Graduate Studies

The Effectiveness of Tight Glycemic Control on Reducing Surgical Site Infection in Diabetic Patients Undergoing Coronary Artery Bypass Grafting

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Dedication

منذ الخليقة وجد الإنسان نفسه على وجه الأرض لا يستطيع العيش بمعزل عن الآخرين، ونجد بجميع مراحل حياتنا من هم يستحقون منا كل الشكر والتقدير فلهم علي فضل كبير قد يبلغ عنان السماء، فقد كان وجودهم سبب في فلاحي ونجاحي بهذه الدنيا وبالآخرة أيضًا.

أن قاطرة بحثي هذا قد مرت بالعديد من العوائق والصعوبات، وعلى الرغم من هذا فأني حاولت أن أتخطى كل هذه العقبات والصعوبات بثبات شديد بفضل الله سبحانه وتعالى، وبفضلكم انتم

إليك أنت وحدك يا صاحب السيرة العطرة وصاحب الفكر المستنير، فأنت وحدك من كان له الفضل الأول على لأبلغ التعليم العالي، لك أنت والدي الحبيب الذي أتمنى من الله أن يطيل عمره.

إليك أنتِ يا من وضعتني على طريق الحياة، فأنتِ من جعلتني ربط الجأش، ويا من راعيتني حتى صرت رجل كبير، لك أنتي يا أمي الغالية.

إلى جميع أخواتي الذين كان لهم الفضل في إزالة الكثير من العقبات والصعوبات من طريقي، أليكم أساتذتي الكرام، فكنتم دائمًا تقدمون لي يد العون.

دائمًا ما نسير في دروب الحياة، ويبقى معنا من يسيطر على أذهاننا في كل طريق نسلكه، إليكِ أيضًا زوجتي العزيزة ورفيقة الحياة والكفاح

إلى جميع أصدقائي الذين كانوا دائمًا بالنسبة لي بمثابة العضد والسند حتى أستطيع أن استكمل البحث.

ولا يمكن أن أنسى أساتذتي الكرام الذين كان لهم الفضل الكبير والدور الأول في مساندتي وتوضيح لي العديد من المعلومات الهامة والقيمة بالنسبة لي.

فأنا اليوم أقوم بإهداء لكم هذا البحث وأنا أتمنى من الله أن يطيل لي في أعماركم ويرزقكم دائمًا بالخيرات.

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الإقرار

أنا الموقع أدناه مقدم الرسالة التي تحمل العنوان:

The Effectiveness of Tight Glycemic Control in Reducing Surgical Site Infection in Diabetic Patients Undergoing Coronary Artery Bypass Grafting

أقر بأن ما اشتملت عليه هذه الرسالة إنما هي نتاج جهدي الخاص، باستثناء ما تمت الإشارة إليه حيثما ورد، وأن هذه الرسالة ككل، أو أي جزء منها لم يقدم لنيل أية درجة أو لقب علمي أو بحثي لدى أية مؤسسة تعليمية أو بحثية أخرى.

Declaration

The work provided in this thesis, unless otherwise referenced, is the researcher's own work, and has not been submitted elsewhere for any other degree or qualification.

Student's Name: بلال رباح حسين بلاصي **اسم الطالب:**

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Date: 2024/5/6 **التاريخ:**

List of Contents

List of Table

List of Appendices

List of Abbreviations

AACE	American Association of Clinical Endocrinologists
ACS	Acute Coronary Syndrome
ADA	American Diabetes Association
BG	Blood Glucose
CABG	Coronary Artery Bypass Grafting
CABG	Coronary Artery Bypass Grafting
CDC	Centers for Disease Control and Prevention
CHD	Coronary Heart Disease
COPD	Chronic Obstructive Pulmonary Disease
DM	Diabetes Mellitus
HbA1c	Hemoglobin A1c
ICU	Intensive Care Unit
LOS	Length Of Stay
NICE	The National Institute for Health and Care Excellence
RCT	Randomized Controlled Trial
SSIs	Surgical Site Infections
SWI	Sternal Wound Infection
TGC	Tight Glycemic Control

The Effectiveness of Tight Glycemic Control in Reducing Surgical Site Infection in Diabetic Patients Undergoing Coronary Artery Bypass Grafting

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Abstract

Introduction: mellitus is associated with increased surgical morbidity and mortality. The relatively high risk may be related to the level of perioperative hyperglycemia. Glycemic control in postoperative cardiac patients is necessary to improve the outcome of wound infection and overall mortality. In recent years, clinical trials that evaluated blood glucose control in critically ill patients for intensive blood glucose management and found a significant reduction in morbidity and mortality. Some organizations have published recommendations for the management of blood glucose in critically ill patients that reflect this information. However, new clinical trials evaluating blood glucose target areas in critically ill patients have found conflicting results, leading to a reassessment of current targets and guidelines, enabling less strict blood sugar target areas. With the inconsistency in clinical trials evaluating a target blood glucose range for critically ill patients, especially postoperative cardiac surgery patients, target blood sugar is still not clearly defined. Further comparisons of specific glucose ranges would allow a clearer definition of recommended blood glucose targets for postoperative cardiac patients.

Aim: The aim of this study is to evaluate the efficacy of tight glycemic control interventions intraoperative and postoperative with a continuous insulin infusion to maintain blood glucose levels of 150-180 mg/dl to reduce the complications of open heart surgery, ie. readmission, hospital mortality, length of stay, hospital stay, incidence of hypoglycemic events (blood glucose levels ≤70 mg/dl) in adult diabetic patients undergoing CABG.

Material and method: A quasi-experimental study conducted among diabetic patients undergoing elective CABG. Single-center clinical trial conducted among diabetic patients, male 86 and female 14, aged 18-70 years with ASA II- III undergoing CABG from AL-Ahli Hospital, Hebron-Palestine. Patients are divided into experimental group (E group) modified tight control (Blood Sugar maintained between 150-180 mg/dl) and ahistorical Control Group (C Group) received sliding-scale insulin to maintain blood glucose). Patients were followed up to 48 hours postoperatively. Incidence of surgical site infections, readmission, in-hospital mortality, length of ICU stay, length of hospital stay, incidence of hypoglycemic events (blood sugar levels ≤70 mg/dl), and another complications in adult diabetic patients undergoing CABG were collected.

Results: There are no significant differences between the historical group and the experimental group in gender, age, weight, high, and BMI (P-values>0.05). The results exhibited that there were no significant difference in the mean of preoperative blood glucose in the historical group M±

SD(185.22±38.76) compared to the experimental group173.72±18.74 (p= 0.063). At the opposite of this result, the results exhibited that the mean of hemoglobin A1c in the historical group (mean=9.12) is significantly lower than that in the experimental group (mean=9.71) (p=0.003).

The results exhibited that the mean of intraoperative blood glucose in the historical group M± SD (223.03±47.32) is significantly higher than that in the experimental group M± SD (170.91±2.64) (p=0.000).

The results exhibited also that the mean of postoperative blood glucose in the historical group (mean=283.08) is significantly higher than that in the experimental group (mean=168.88) (p=0.000).

The results exhibited that the number of patients who had deep sternal infection in the historical group (N (%) =4(8%)) is significantly higher than that in the experimental group (N(%)=0(0%)) (p= 0.041). Also the results exhibited that the number of patients who had pneumonia in the historical group (N(%)=4(8%)) is significantly higher than that in the experimental group (N (%)=0(0%)) (p= 0.041). Also the results exhibited that the number of patients who had stroke in the historical group(N(%)=4(8.2%)) is significantly higher than that in the experimental group(N(%)=0(0%)) (p=0.039) .

The results exhibited that the mean of ICU-LOS (days)in the historical group (mean=4.14) is significantly higher than that in the experimental group (mean=2.18) (p=0.000). Also, the results exhibited that the mean of postoperative hospital LOS (days) in the historical group (mean=5.72) is

significantly higher than that in the experimental group (mean=4.98) (p=0.000).

Conclusion : Maintaining blood glucose levels (150-180) with continuous insulin infusion at all stages of the perioperative period will minimize the incidence of surgical site infection, episodes of hypoglycemia, stroke, pneumonia and length of stay in ICU and hospital in patients undergoing CABG surgery.

Key words: CABG, Cardiac Surgery, Surgical Site Infection, Glycemic Control, Insulin, hypoglycemia, hyperglycemia.

Chapter One

The Introduction

1.1 Background

Increased surgical morbidity and mortality were combined with diabetes mellitus. The high risk may be associated with perioperative levels of hyperglycaemia. Approximately 30-40% of coronary heart disease (CHD) patients with coronary artery bypass graft with metabolic syndrome or diabetes mellitus (DM) are at risk for hyperglycemia (Gorter et al., 2004). Hyperglycemia results in increased susceptibility to surgical wound infection, brain damage, heart damage and death (Eagle, et al., 2004; Kubal, et al., 2005). Hyperglycemia is a significant cause of the development of irregular proteins through non-enzymatic glycosylation, leading to neurological damage, brain chemistry, disrupting cell metabolism through aerobic glucose-lactose conversion (Doens et al. 2005). In addition, hospitalization and costs increase through hyperglycemia (Whang, et al., 2006).

Van Den Berghe and colleagues (2001) showed a reduction in mortality while keeping blood glucose (BG) between 80 to 110 mg/dL, the idea of tight-glycemic control (GC) became more common. Data have reported that hyperglycemia among ICU patients is associated with increased death and infection (Bagshaw et al., 2009; Falciglia et al., 2009).

Compared with non-diabetic patients who have chronic heart disease in several vessels leading to invasive revascularization procedures, such as

(CABG), patients with diabetes mellitus have a two to four times more chance of developing CHD (Deb, et al 2013). Among the nearly 397,000 open heart surgeries in the United States, up to 31% of patients experience hospital-acquired infections within 1 month of procedures, (Mozaffarian, 2015).

Surgical infections risk factors after the Open heart procedure are diabetes mellitus, obesity, high serum glucose levels preoperative (≥ 200 mg/dL) and female gender (Fowler et al., 2005). During the immediate (≤48 hours) postoperative period, serum glucose levels ≥200 mg/dL led to an increased risk of surgical infections (Lee et al., 2014; Furnary et al., 2004). Improper glycemic control preoperative leads to poor control during and after hospitalization and will result in increases the incidence of problems such as Improper wound healing and higher frequencies of surgical infections and finally increased hospitalization and increased mortality (Engoren, et al. 2014).

Increased re-hospital stay in patients can be used as low quality of care and a product of inadequate treatment, Improper care for underlying problem, poor discharge coordination service, incomplete preparation for discharge and poor access to care (Halfon, et al. 2006, Goldfield et al., 2008). Within 30 days of the CABG service, Hannan et al (2013) showed 16.5 percent re-hospitalization and Horwitz et al (2015) a re-hospitalization rate of 13.2%. Postoperative infection was reported as the most common cause of re-hospitalization rate by the authors of both studies.

The American Association of Clinical Endocrinologists (AACE) and the American Diabetes Association (ADA) recommend intravenous insulin infusions to address the issue of insufficient glycemic control in acutely ill patients with diabetes to achieve and maintain stable glycemic control in critically ill patients with DM (Moghissi). , et al., 2009). For the treatment of chronic hyperglycemia in critically ill patients with a target glucose of 140-180 mg/dL, it is recommended to start insulin infusion with a blood glucose limit not exceeding 180 mg/dL for most of these patients. (American Association for Diabetes, 2015). The ADA guidelines reported that a target blood glucose level of 110-140 mg/dL may be sufficient for selected patients who is critically ill without an increased risk of hypoglycemia and proposed baseline and corrective doses of subcutaneous insulin in non-critically ill patients with a target of ≤ 140 mg/dL blood glucose level. There're no defined guidelines, but which identify a desirable target area for maximum blood glucose level postoperatively. Founded in 2003 as a working to improve the safety of surgical care in national quality alliance of organizations by eliminating postoperative complications, the Health Improvement Project developed a key measure to maintain blood sugar levels at 180 mg/dL during the preoperative and postoperative periods depend on evidence-based practice to reduction in surgical infections. The Society of Thoracic Surgeons also recommends a target of 180 mg/dL in the immediate postoperative period. (Lazar, et al., 2009). In comparison, randomized clinical trial (RCT) conducted in the Portland Diabetes Project in a of 5510 diabetic patients with heart surgery tested the effects of intravenous insulin standard protocol for maintaining blood glucose level at 150 mg/dl. They found that use of this procedure was safe and linked with reduction in surgical infections by 77 percent (Furnary, et al., 2006).

In review done in 2009 of the postoperative effects of strict glycemic regulation by Kao et al. Five randomized clinical trial included 773 adult diabetic patients who under-went a number of surgeries. The investigators found that the use of continuous insulin infusions with strict glycemic control to minimize infections at surgical sites was not confirmed by adequate evidence.

Aggressive glycemic regulation has been shown to improve clinical outcomes for critically hospitalized patients, especially for CHD patients (Furnary et al., 2006; Trence, Kelly, & Hirsch, 2003). Recent findings showing that there is little change in health outcomes or perhaps worse outcomes for critical patients treated with active glycemic control have questioned these data, which also reduces perioperative disease and increases short- and long-term survival. There are no clear recommendations for cardiac surgeons for how the optimal amount of glucose should be during the perioperative cycle and the safest method to reach these target levels, beyond the obvious knowledge about the importance of glycemic regulation (Arabi et al., 2008; Finfer & Heritier, 2009; Chan et al., 2009; Gandhi et al., 2007; Lazar et al., 2011; Griesdale, et al., 2008; Wiener, Wiener, & Larson, 2008).

New study results have led to change their recommendations to more restrictive blood glucose level parameters. The Institute for Health Care Development (IHI, 2011) put recommendation that cardiovascular surgery patients were at high risk from complications resulted from hyperglycemia during the first two postoperative days keep blood sugar levels below 180 mg/dl for management. The American Diabetes Association (ADA, 2012) suggests starting insulin therapy with a maximum threshold of 180 mg/dl for chronic hyperglycemia. Blood sugar levels should be monitored from 140 to 180 mg/dl in chronically ill patients until initiating insulin therapy (ADA, 2012). For selected patients, stricter targets, such as 110-140 mg/dl, may be acceptable, as long as this is done without severe hypoglycaemia (ADA, 2012). Many improvements related to glucose metabolism are correlated with the preoperative phase. Hormones grow, such as adrenaline, cortisol and glucagon, resulted to increase gluconeogenesis. increased insulin tolerance combined with previous causes, and reduction in insulin secretion, put patients underwent surgery at high risk to develop hyperglycemia. Decreased phagocytosis, delayed chemotaxis, deviations in granulocyte adhesion and depressed bactericidal potential are correlated with perioperative hyperglycemia (Hanazaki, et al., 2009). The level of hyperglycemia has been shown to affect phagocytic activity and thus increase the infection as low as 200 mg/dL (MacRury et al., 1989; MacRury et al., 1989). Insulin exhibits potent and acute anti-inflammatory activity by inhibiting tissue factor, the intranuclear factor kB and plasminogen activator inhibitor-1. Surgical site infections have major effects including multiple organs failure and increasing mortality. An important function, not only in the regulation of blood glucose (BG) but also as an anti-inflammatory and antioxidant (Lipshutz et al., 2009). The aim of this study is to evaluate the efficacy of tight glycemic control interventions intraoperative and postoperative with a continuous insulin infusion to maintain blood glucose levels of 150-180 mg/dl to reduce the complications of open heart surgery, ie. readmission, hospital mortality, length of stay, hospital stay, incidence of hypoglycemic events (blood glucose levels ≤70 mg/dl) in adult diabetic patients undergoing CABG.

1.2 Statement of Problem

For cardiothoracic surgical teams and clinics, postoperative site of infection in the open-heart surgeries is a serious problem. In cardiovascular surgical patients including CABG surgery or valve replacement surgery, there is insufficient literature on the effect of intraoperative glycemic regulation on wound infections at surgical sites. There is minimal evidence that the insulin regimen and / or blood glucose benefit is safe and effective in stability blood glucose level or the prevention of surgical site infections (SSIs) during the intraoperative period. Patients undergoing open heart surgery require a better understanding of glycemic regulation during the intraoperative phase and its effect on postoperative surgical infection.

Several studies have shown that hospital mortality has a higher risk for patients with acute coronary syndrome who have hyperglycemia (Meier, et al., 2005). Hyperglycemia is crucial for evaluating the outcome of acute coronary heart disease in diabetic and non-diabetic patients. Cheung, et al., (2006) and Svensson, et al., (2006) analyzed the results of 6,280 patients who underwent cardiac surgery and reported higher intraoperative morbidity and mortality in patients with blood glucose levels ≥ 360 mg/dl (Doenst, et al., 2005). Related effects have been shown in increased postoperative complications due to higher blood sugar levels (Gandh, et al., 2005; Duncan, et al., 2010). The results have clearly suggested that elevated blood sugar levels lead to higher postoperative morbidity and mortality in patients with and without diabetes undergoing cardiac surgery during the preoperative phase. In diabetic patients, the incidence of cardiovascular disease is higher. By comparison, decreased platelet function, fibrinolytic function, and decreased endothelial function are more prominent in these patients, leading to lower graft patents, higher preoperative mortality, and reduced short- and long-term postoperative survival (Carson, et al., 2002). By inhibiting proinflammatory factors and reducing inflammatory mediators, insulin acts as an anti-inflammatory agent (Langouche, et al., 2005). Insulin controls the pathway of L-arginine nitric oxide, which improves vasodilation and endothelial activity and increases the release of prostacyclin, improving platelet function. On the other hand, apoptosis with insulin decreases (Gao, et al., 2002). Many studies on populations have shown that lower infection rates, shorter residence time (LOS) and faster recovery are correlated with glycemic regulation strictly during surgery (Lazar, et al., 2004)

1.3 Significance of the study

After cardiac surgery, hyperglycemia is common, although international evidence sufficiently supports the negative effect and association with poor health problems. Good regulation of blood glucose level during the first 48 hours after admission to ICU following cardiac surgery tends to correlate with significantly reduction in early mortality, also results that illustrates the importance of strict glycemic control. In the early postoperative phase, a less restrictive insulin infusion procedure was used which aimed at achieving adequate glycemic control tends to be substantially safe and effective. The inconsistent results in the literature show the need for more studies. The value of intensive blood glycemic regulation and its potential positive effects on patients with heart surgery must be discussed in future randomized controlled trials.

The literature provides that there is a greater risk of elevated morbidity and mortality in patients who undergo postoperative wound infections following open heart surgery. Postoperative wound diseases also improve LOS in the hospital and raise costs. Ways to reduce the prevalence of these diseases, resulting in high morbidity and mortality, need to be sought.

A correlation between low glycemic control and surgical infection rate has been indicated by previous studies that have examined surgical infections in open heart surgery. Many of these experiments, without randomization or reference groups, are retrospective patterns. There is minimal literature examining perioperative glycemic regulation, and the results of these studies are unpredictable. In open heart surgery, it is unclear whether strong glycemic control is beneficial in the perioperative phase.

Research is required to explore whether the association between hyperglycemia and surgical infection is a causal relationship and to establish the impact of tight glycemic control on postoperative surgical wound infections.

It is also important to evaluate the close glycemic regulation of the diabetic patients compared to the non-diabetic patients associated with postoperative infections, and to define levels of blood glucose that provide optimal outcomes in for diabetic and non-diabetic patients.

Finally, it is necessary to decide if continuous intravenous insulin infusion to control blood glucose levels during the perioperative time is more efficient in controlling glycemia than intravenous insulin bolus injections.

This study will investigate the effects of a strict glycemic control protocol during the intraoperative and postoperative period up to 48 hours postoperatively on postoperative SSIs in patients undergoing CABG surgery.

1.4 Aim of the study

The aim of this study is to evaluate the efficacy of tight glycemic control interventions intraoperative and postoperative with a continuous insulin infusion to maintain blood glucose levels of 150-180 mg/dl to reduce the complications of open-heart surgery, ie. Readmission, hospital mortality, length of stay, hospital stay, incidence of hypoglycemic events (blood glucose levels ≤70 mg/dl) in adult diabetic patients undergoing CABG.

1.4.1 Primary objectives

To determine the effectiveness of tight glycemic control to reduce infections at surgical sites

1.4.2 Secondary objectives

- To identify the effectiveness of tight glycemic control to reduce ICU and hospital LOS
- To identify the effectiveness of tight glycemic control to reduce hospital mortality
- To identify the effectiveness of tight glycemic control to reduce complications postoperatively.

1.5 Research questions

Does tight glycemic control reduce surgical site infection in diabetic patient undergoing CABG?

Does tight glycemic control reduce ICU and hospital LOS in diabetic patient undergoing CABG?

Does tight glycemic control reduce in-hospital mortality in diabetic patient undergoing CABG?

Does tight glycemic control reduce complications in patient undergoing CABG?

1.6 Research Hypothesis

- There is a significant difference at a level of 0.05 related to the tight glycemic control and reducing surgical site infection in diabetic patient undergoing CABG.
- There is a significant difference at a level of 0.05 related to related to the tight glycemic control and reducing ICU and hospital LOC.
- There is a significant difference at a level of 0.05 related to the tight glycemic control and reducing in-hospital mortality rate in diabetic patient undergoing CABG.
- There is a significant difference at a level of 0.05 related to the tight glycemic control and reducing complications in diabetic patient undergoing CABG.

Chapter Two

Background

2.1 Background

A review of the literature relevant for a strict glycemic control effect on the incidence of infection at surgical sites in patients undergoing cardiovascular surgery is discussed in this chapter. The literature review focused on the prevalence and the incidence of SSIs in patients with open-heart surgery, the effects of hyperglycemia and diabetes on surgical infections, biomarkers commonly used to classify surgical infections, and existing postoperative, perioperative and intraoperative research related to strict glycemic control. Existing research gaps so far have also been examined. The databases used for literature search include: PubMed; MD Consult; ;Cochrane database and Cumulative Nursing and Allied Health Literature Index (CINAHL);. "glycemic control", ",Blood glucose", "level of blood glucose "hyperglycaemia" and "hypoglycaemia" were the words in the pursuit of glucose. " sternal wound infection (SWI)", and "Surgical site infection (SSIs)" were the keywords for infection. " open heart surgery", Cardiovascular surgery", "coronary artery bypass grafting (CABG)," cardiac surgery "and" valve replacement surgery "were included in the search terms for open heart surgery." "insulin protocol" "insulin drip" "Insulin infusion", "insulin intervention" and "glucose-insulin-potassium drip" were the keywords for glycemic control intervention. "Infectious biomarkers", "procalcitonin", "C-reactive protein", and "postoperative infection markers" were the keywords for infection biomarkers. Documented research treating postoperative SSIs and open-heart surgery in patients with diabetic patients or have hyperglycemia has most often been found in medical journals, especially in cardiothoracic surgery, endocrinology, and anesthesiology. The assignment was limited to studies in adults on humans who explicitly looked at blood sugar levels before, intra and postoperatively, and wound infections in heart surgery patients. Although the main focus of this study was cardiovascular surgery, other research related to glycemic regulation in critically ill patients was reviewed and integrated. In addition, the research studies were limited to those publication date of 1998 or later and had been conducted in English.

2.2 Diabetes Mellitus

“Diabetes mellitus is a metabolic condition characterized by chronic hyperglycaemia due to lack of insulin secretion, increased insulin resistance or a combination of both. Type 2 diabetes mellitus is mainly attributed to insulin resistance due to many etiologies, including genetic predisposition, unhealthy diet, lack of physical activity and a characteristic central trend of weight gain, involving 90% -95% of all patients diagnosed with diabetes. Approximately 28% of diabetics undergo bypass surgery” (ADA. 2013).

In diabetic patients, the incidence of kidney failure, strokes, and sinus infections is greater (Leavitt, et al., 2014). Regardless of the cause, diabetic patients have a 44% higher risk of readmission (after hospitalization after coronary surgery) and have 24% higher risk of hospital readmission for heart complications than the corresponding non-diabetic patients who underwent open heart surgery (Herlitz, al. 2000).

2.2.1 Diabetes and cardiac disease

Insulin resistance and hyperglycemia contribute to an endothelial dysfunction, transition of metabolized free fatty acid, and subsequent thrombogenesis (Johnstone, et al., 2013; Steinberg, et al., 2017). Endothelial dysfunction triggered by hyperglycemia is due to an imbalance between the bioavailability of nitric oxide and aggregation of reactive oxygen species, resulted from protein kinase C activation. superoxide anion generation also causes of the Hyperglycemia, which inactivates peroxynitrite to form nitric oxide, which induces nitrous oxide (Johnstone, et al., 2013). A good prediction for hgroupful nitrogen oxide results is the reduced availability of nitrogen oxides (Lerman & Zeiher, 2015). endothelin-1 developed from Protein kinase C, which induces platelet aggregation, vasoconstriction, vascular inflammation (Geraldes & King, 2010).

Production of advanced glycation products CAGE surface receptor RAGE resulted of Hyperglycemia. By activating three main transcription factors, RAGE leads to the inflammatory response: activated protein-1, nuclear factor KB, and early growth response, all these of which are inhibited under normal insulin conditions (Schmidt, et al., 1999). Dysfunction in Endothelial also results in an increase in vasoconstrictor and synthesis of prostanoid. With increased concentrations of free fatty acids and inflammatory markers, increased weight, a typical trait in diabetics, is closely correlated (Shulman, et al., 2016). By growing apolipoprotein B, triglycerides, and low-density lipoproteins, insulin resistance also facilitates atherosclerosis. Furthermore, lipoprotein concentrations with very low density are produced in response to increased apolipoprotein B synthesis (Zhang, et al., 2012). The result of a prothrombotic condition was coronary heart disease in diabetics. Under normal conditions, circulating insulin concentrations inhibit platelet aggregation and thrombosis by inhibiting tissue factor and by inhibiting the development of plasminogen activator inhibitor-11 (PAI-1). Insulin resistance, on the other hand, promotes increased PAI-1 and fibrinogen synthesis as well as decreased production of tissue plasminogen activators. Taken together, these variables result in atherothrombosis (Chaudhuri, et al., 2004). A recently described class of micro-RNAs (miRNAs) that regulate gene expression at the transcriptional level is a significant contributor to hyperglycemia-induced vascular injury (Shantikumar, et al., 2010).

Diabetics show that miRNAs involved in angiogenesis, vascular repair, and endothelial function are significantly downregulated (Zampetaki, et al., 2010). Finally, increased oxidative vascular stress induces plaque failure, decreased platelet function, and thrombosis, resulting in decreased graft patent, decreased ischemic event, and increased incidence of recurrent revascularization (Lazar, 2009).

Following acute myocardial infarction, acute coronary artery disease, or coronary artery surgery, hyperglycemia is linked with poorer outcomes. A meta analysis of 20 researches of undiagnosed diabetic patients with glucose concentrations ≥110 mg/dL was performed by Capes and colleagues (2014). The risk of mortality in such patients was 3.9 times higher than in non-diabetic patients with lower glucose concentrations.

Glucose levels above 180 mg/dL were linked with an increasing risk of cardiogenic shock and heart failure in patients without diabetes. There was a marginally increased risk of death in patients with DM in their concentrations of glucose ≥180 mg/dL (Capes, et al., 2014). Kosiborod, et al. (2018) examined glucose absorption levels in 141,680 elderly patients in hospitals with acute myocardial infarction. In the patients who had glucose levels equal or greater than 240 mg / dL, 25 percent were not diagnosed with DM. Increased blood suger levels were linked to cause higher risk of death in patients not previously diagnosed with DM (10% -39%) compared with those with DM (16% -24%). Foo, et al., (2013) found a strong correlation between high serum glucose levels and elevated occurance of left ventricular heart failure and death. In another study of 2126 patients with ACS. Data from 227 DM patients and 287 patients without DM diagnosed with acute MI were analyzed by Meier et al (2005). In both patients with diabetic and without-diabetic hyperglycaemia at the time of MI was linked with higher infarct time, shorter survival, , and increased incidence of adverse events.

The link between diabetes and mortality was analyzed by Gandhi, et al (2017) in their study glucose measurements analyzed from patients underwent cardiac surgery and results from 410 patients found that high level of glucose concentration of 20 mg/dL in the mean intraoperative was correlated with a 30% increase in adverse reactions.

Kubal, et al (2005) in 6000 patients who underwent CABG. In insulin dependent DM patients linked with an more incidence of deep SSIs (adjusted OR =2.96), renal failure (adjusted OR =4.5), and postoperative prolonged stay (adjusted OR = 1.60).

In a retrospective study of Doenst, et al (2005) 6,290 patients with open-heart surgery, found that a maximum glucose of ≥ 360 mg/dL was correlated with an increased risk of side effects and mortality. Ascione, et al (2008) In thier retrospective study of 8727 patients with cardiac surgery, found that glucose levels ≥ 200 mg/dL were correlated with an increased risk of hospital morbidity and mortality sometime during the first 5 postoperative days. Taken together, these results show that the risk of morbidity and mortality increases with hyperglycemia in acute coronary artery syndrome after heart surgery.

In the publications mentioned by Furnary et al (2014), the Portland Diabetic Project provides clear evidence of a negative correlation between hyperglycemia in diabetics undergoing cardiac surgery. 4864 diabetics registered in the non-randomized but still potential intervention experiment. The reviewers focused on the associations between use of continuous insulin infusion and the incidence of deep SSIs, mortality and hospitalization period. To increase the risk of perioperative mortality, hyperglycemic state was shown to be an independent variabel. Compared with DM patients whose blood glucose was 'out of control', patients with blood glucose ≤150 mg/dl, 57% less mortality, 66% less likely to developed deep SSIs.

A prospective randomized study was performed by Butterworth et al (2017) on 380 patients without DM underwent CABG, and maintain blood glucose levels during intraoperative ≤100 mg/dL receiving a continuous insulin infusion while no insulin was obtained by the other group. Despite the fact that the group who receiving insulin had significantly lower intraoperative glucose levels, there was no differences in neuro-psychological morbidity or neurological or mortality between the both groups.

In critical patients Hyperglycemia was associated with adverse effect postoperative. Van den Berghe, et al., (2014) conducted A milestone analysis of 1548 ventilated patients. If the blood sugar exceeded 215 mg/dL and had a target range of 180-200 mg/dL, one group received a continuous insulin infusion insulin to maintain a blood glucose level between 80-110 mg/dL while the other group received. While infusion insulin therapy significantly reduced mortality in patients with ICU needs of more than five days, there is no effect in mortality or morbidity in patients with ICU needs in less than 3 days.

4660 patients with perioperative hyperglycemia or known diabetes who underwent a possible CABG surgery were reviewed by Bhamidipati et al., (2011). In this study, patients were divided into three groups in which the first blood glucose level maintained ≤126 mg/dL in control group and the second group blood glucose level labeled moderate group and the third group blood sugar levels ≥ 181 mg/dL labeled liberal group. In the dense and moderate group, the lowest mortality was 2.0 per cent against 2.9 per cent. The incidence of the risks of major complications was lower in the moderate group, must suggest that moderate hyperglycemia 128-180 mg / dL may be appropriate for DM patients undergoing relevant coronary heart disease.

2.2.2 The effect of SSIs on patients outcome

Complications occurs postoperative such as surgical site infections can adversely affect the quality of life of patient's (Badia, et al. 2017).

SSI can cause significant mortality and morbidity, associated with prolonged hospital stay after surgery, elevated medical costs and endangered health effects (Anderson, 2014; Nabor et al., 2015; Newman, 2015; Junker, et al. 2012; Lipke & Hyott 2010). In addition, the patients and their family’s members become more upset if their patient is hospitalized for a longer period (Badiaa, et al. 2017). Other studies have shown similar results, showing that patients who developed SSIs are more risk to die, 60% higher risk to be in an ICU and up to 5 times more likely to re-hospitalization (Kirkland, et al. 2009). SSI occurs during surgical procedures in the surgical area and has a negative impact on the subsequent care of patients. In fact, Around 5% of patients undergoing open-heart surgery have SSIs. (NICE, 2008: Leaper, et al. 2013). The effect of surgical site infections should therefore not be under-estimated (Nessem, et al. 2012), as they eventually have a significant influence on a patient's postoperative outcomes (NICE 2008). In fact, SSI can present life-threatening complications after surgery, and patients who develop an SSI are more likely to spend an estimated 7 to 10 days in the hospital (NICE, 2008). In postoperative patients, SSI is still an extremely complicated problem (Al Maqbali, 2016).

2.2.3 Pathophysiology of surgical infections

In a healthcare environment, SSIs are the result of interaction between microorganisms, a compromised host and a transmission chain. Such an infection occurs when, via surgical incision, microorganisms are introduced as a result of fungus or bacteria that migrate from the patient's GI system or patients skin as endogenous infection such as microflora or direct transmission to healthcare professionals from surgical instruments. It might happen through the airways (exogenous infection) (Harrington, 2014). The incision site becomes infected when microbes enter the wound and SSI creates (Harrington, 2014). Bacteria can travel through the bloodstream through the body and in other cases, prosthetic implants or deposits on can be also another the source of infections (Harrington, 2014).

2.2.4 Contributing risk factors for infections at surgical sites

In surgical patients, the literature illustrates several risk factors for SSI. Variables for surgical procedures are classified into two groups: surgical procedures related risk factors and patients related risk factors. The initiation of SSI has been correlated with many patient-related risk factors, such as existing infections, malignancies, shock, diabetes mellitus, respiratory failure, trauma, hypothermia, hyperglycemia, hypoxia, immunodeficiency, obesity, malnutrition, old age, and smoking (Apisarnthanrk et al. 2003; Barnes, 2015; Barbsa & Silva 2012; Lepelletier, et al. 2013; Reyes, et al. 2011). The same, surgically procedure includes steps such as careful preparation and draping for surgery, minimizing the duration of preoperative hospitalization, use of personal protective equipment (PPE), preventing removal of the patient's hair, or, if absolutely necessary, washing with antiseptics, adequate preoperative medication (Barnes 2015; CDC 2011; Lepelletier, et al. 2013; Mc Hugh et al. 2014; Oliveira & Gama 2015).

Many studies trying to identifies SSIs risk factors related to cardiac surgery, associated risk factors included a diagnosis of DM (Ariyaratnam, et al., 2010; Harrington, et al., 2004; Ji et al., 2009; Fusco, et al., 2016; Elola, et al., 2011), high age over 65 years (Ariyaratnam et al., 2010; Borger et al., 2015; Ji et al., 2019) , obesity (Ariyaratnam et al., 2010; Olsen et al., 2002; Harrington et al., 2004), male sex (Borger et al., 1998; Spelman et al., 2000), female sex (Paletta, et al., 2000; Harrington et al., 2004), chronic obstructive pulmonary disease (COPD) (Ariyaratnam, et al. , 2017) and impaired renal function (Toumpoulis, et al., 2015). The predominant risk factors identified for SSI in open-hearted patients included obesity and diabetes mellitus diagnosis.

2.3 Evidence-based Guidelines recommended for the management of hyperglycemia for the patients with DM undergoing cardiac surgery

2.3.1 Blood sugar control for cardiac surgery patients

In 2009, update published by the Society of Thoracic Surgeons recommendations to avoid complications, particularly deep-seated infections in sternum wound such as prescribed blood sugar thresholds of ≤180 mg/dL during surgical procedure and immediate postoperative period. Following the launch of the NICE SUGAR study, several studies carefully examined moderate glycemic control in patients undergoing cardiac surgeries. The results of cardiac surgery also encourage moderate glycemic regulation (Lazar, et al., 2011; Bhamidipati, et al., 2011; Desai, et al., 2012). In their randomized controlled trial, Desai et al. (2012) found that liberal glycemic control (121 to 180 mg/dL) in CHD patients with was associated with less hypoglycemia compared with strict glycemic control.

In their randomized controlled trials, Lazar et al. (2011) reported fewer incidents of hypoglycaemia and no significant side effects in patients with diabetic heart surgery who received an insulin infusion regimen with a blood glucose target of 120 to180 mg/dL compared to 90 to 120 mg/Dl.

Bhamidipati, et al. (2011) In their quasi-experimental research of 4600 patients underwent cardiac surgery, moderate glycemic control (127 to 179 mg/dL) observed superior robust glycemic control (less than 126 mg/dL) with lower mortality and morbidity in patients with documented DM or perioperative hyperglycemia.

2.3.2 Adverse effect of hyperglycemia during intraoperative period

Fish, et al. (2003) identified that elevated blood glucose level during surgery seemed to be an independent linked with mortality in patients diagnosed with DM or not. The relevance of blood glucose levels in the during surgery and immediate postoperative cycle to predict morbidity in 200 consecutive coronary artery diseases was retrospectively analyzed by. Serum glucose levels postoperatively ≥250 mg/dL were associated with 10 times likely to increase complications of heart surgery. In a retrospective review of 291 patients who underwent CABG surgery, McAlister and co-workers (2003) published similar results. On the first postoperative day, the mean serum glucose level significantly predicted the production of a negative result. A retrospective systematic review of 409 patients with cardiac surgery by Gandhi and colleagues (2005) has documented adverse effects of high blood sugar levels intraoperative.

An associated independent risk factor for intraoperative complications, including mortality, was intraoperative hyperglycemia. Prior to surgery, irregular glucose readings may also be a predictor of reduced postoperative survival. The effect of high blood glucose levels on the function of a group of 1375 CABG patients was studied by Anderson and colleagues (2005). There were one-year deaths in patients with elevated fasting hyperglycemia that were twice higher than patients with normal fasting blood glucose level and equal to those diagnosed with DM. Taken together, these results clearly indicate that higher preoperative glucose levels and maintained elevated postoperative glucose levels are an indication of increased intraoperative mortality or morbidity in patients with and without DM, both during and immediately postoperative. The researcher in the current research review results show that reducing intraoperative glucose levels with insulin treatment reduces mortality and morbidity in patients undergoing cardiac surgery.

2.3.3 Glycemic control Benefits on clinical outcomes

Three thousand five hundred and fifty-four (3554) patients who underwent CABG procedure from 1987 - 2001 participated in the study of furniture, et al (2003). Based on the form of glycemic regulation and the targeted glucose levels, the year of surgery, the patients were classified into three groups. Patients receiving subcutaneous insulin every four hours from 1987 to 1991 to maintain serum glucose ≤200 mg/dL. A constant intravenous (IV) insulin infusion was used between 1991 and 1998 to control serum glucose at between 150 - 200 mg/dL. From 1998 to 2001, the Portland Protocol was introduced, which used a constant drop of insulin to maintain serum glucose between 100 and 150 mg/dl. Continuous infusion of insulin resulted in slightly lower mean glucose levels than sporadic subcutaneous insulin therapy could provide. Since 1992, when continuous insulin procedures were adopted, the perioperative mortality of CABG patients with diabetes decreased by 50 percent (4.5 percent versus 1.9 percent, $p \leq 0.0001$).

The frequency of deep wound infections also decreased sharply ($p \leq 0.001$). The initial sequence for Furnary and Co-workers (2004) was extended to include an additional 1,900 patients treated under the 2001-2005 Portland Protocol. A new glycemic control measurement process called 3-blood sugar or 3-BG was adopted, consisting of the mean of all glucose values measured on the day of surgery and the first and second postoperative day. An independent measure of perioperative mortality ($p \leq 0.001$) was an improvement in 3-BG. The incidence of deep sternum infections, hospitalization, blood transfusions, newly started atrial fibrillation, and decreased cardiac output were also significantly associated with the mean 3-BG.

2.4 Evidence support the insulin role in treatment of patients underwent CABG.

Lazar and colleagues (2004) introduced diabetes with a modified solution of potassium glucose insulin for DM patients underwent CABG surgery.151 received potassium glucose insulin to maintain 120 to 180 mg/dl serum glucose or sliding glucose maintenance ≤250 mg/dl insulin coverage were prospectively randomized. insulin was released at initiation of anesthesia and was continue to 12 hours in ICU. Patients treated with glucosulin insulin had significantly increased glycemic control immediately before cardiopulmonary bypass (169 mg/dL versus 210 mg/dL, $\leq$0.001) and 12 hours after intensive care (134 mg/dL versus 266 mg/dL; P-value $\leq$0.0001). A slightly higher heart index (p $\leq$0.0001) and less need for isotropic help (P-value $\leq$0.05) and pacing (P-value $\leq$0.05) are seen in patients treated with strict glycemic control. A small reduction in inflammation also resulted in better glycemic control (0 percent vs. 13 percent, p $\leq$0.01) and atrial fibrillation (15% versus 60% , P-value $\leq$0.007). All this contributed to a shorter hospital stay (6.5 days compared to 9.2 days, P-value $\leq$0.0003).

Glycemic regulation is important in reducing acute SSIs has been seen in two more studies. In 1585, CABG patients with diabetes, Zerr and colleagues (2007) studied glycemic regulation effects on the incidence of acute SSIs in patients with mean blood glucose levels of 100 to 150 mg/dl, sensitive SSIs increased from 1.3 to 6.7 percent in patients with blood glucose level of 251 to 300 mg/dl.

Hruska, et al., (2015) In thier retrospective analysis found that CABG patients with DM that a constant insulin infusion their blood sugar levels 120 - 160 mg/dL greatly reduced the degree of SSI compared to subcutaneous insulin injections.

2.5 Recommendations for Hyperglycemia Management in the Peri-operative Period Using Insulin Protocols:

- Intermittent IV insulin doses or subcutaneous insulin injections Instead (Level of Evidence = A), glycemic control is better achieved by constant insulin infusions.
- To sustain blood glucose levels of 180 mg/dL (evidence level = B) for at least 24 hours following surgery, all diabetic patients undergoing heart surgery should receive an insulin injection in the operating room.
- The main method of insulin delivery during the perioperative stage is intravenous insulin therapy. This facilitates quick titration, which allows glycemic management during malabsorption, insulin deficiency and resistance cycles (Friedberg, et al., 2006). Choosing a procedure for insulin infusion relies on the department's desires and resources. To ensure the safe and efficient delivery of a treatment, the persons working with the patient must be comfortable using it. The efficiency of a protocol can be measured by outcomes, such as the time it takes to complete the protocol.

2.6 Recommendations for preoperative Management for diabetic Patients:

Class I

Patients with insulin should maintain their dietary insulin (lispro, aspart, glulisine, or regularly) until dinner after the evening before surgery (evidence level = B).

To achieve glycemic management in hospitalized patients following surgery (level of proof = C), scheduled insulin injection with a combination of long-acting and short-acting subcutaneous insulin or an insulin infusion regimen should be done. Both oral hypoglycemic agents and non-insulin diabetes medications should be stored for 24 hours before surgery (evidence level = C).

Hemoglobin A1c (HbA1c) levels should be obtained before surgery in patients with diabetes or other patients at risk for postoperative hyperglycemia (level of evidence = C).

Class II

It is reasonable to keep the blood sugar level at 180 mg/dl (evidence level = B) before the procedure. Prior to surgery, attempts should be made to improve glucose regulation, as insufficient glycemic control before surgery is associated with increased morbidity, including an increased incidence of deep wound infections and prolonged postoperative stay (Furnary et al., 2004; Lazar, et al. 2004). In general, all oral diabetes medicines, especially sulphonylureas (eg glipizide) and glinides, should be stored within 24 hours before surgery. In the absence of food, such drugs can cause hypoglycaemia. Patients receiving insulin and being admitted for surgery should be advised to continue their dose of basal insulin (egglargine, detemir, or NPH) and to maintain their dose of dietary insulin (eg lispro, aspart, glulisine or regularly) unless otherwise indicated by their primary care physician. NPH insulin can be reduced by one-half or one-third before surgery to avoid hypoglycaemia.

Insulin treatment with either intravenous, continuous injection or subcutaneous basal plus fast-acting insulin may be used depending on the availability of any drug for rapid regulation in a hospital patient with hyperglycaemia (glucose constant> 180 mg/dl> 12 hours before surgery). IV insulin therapy is an effective way to get faster regulation for a patient who is noted to be hyperglycemic in the preoperative area of surgery. In patients with a documented history of diabetes (either type 1 or type 2), IV treatment in the preoperative region can be started immediately. To assess the risk of insulin resistance, all preoperative drugs should be tested. Steroids, protease inhibitors and antipsychotic drugs are among them. Finally, when insulin clearance is compromised and the risk of hypoglycaemia increases, patients with renal insufficiency should be identified. Hemoglobin Alc (HbA1c), a glycosylated hemoglobin, is an exact measure of glycemic regulation over a period of 2 months and 3 months. Adequate glycemic control associated with HbA1c $\leq$7% has been documented by the American Diabetes Association (Kao, et al., 2009).

Optimization of glycemic control in patients with elevated HbA1 makes it possible to achieve an HbA1c prior for surgery in diabetic patients or patients at risk of postoperative hyperglycemia.

2.7 Previous Studies

Zadeh & Azemati (2020) conducted a double-blind randomized clinical trial comparing modified strict glucose control with traditional glucose control in patients underwent CABG in Iran, from 2017 to 2018. The results showed no major variations between primary and secondary outcomes. In the control group there was increase in sternal SSI (7 patients) than in intervention group (1 patient) (P-Value ≤ 0.05). There were no variations between the other complications in both groups. In both groups, the incidence of hypoglycaemia was low. In the intervention, hypokalemia was significantly higher than in the control (P-Value ≤ 0.001). The results showed that the used of adjust tight glycemic control during cardiac surgery can reduce occurrence of hypoglycemia and thus reduce side effects of hypoglycemia. In addition to reducing hyperglycemic risks such as infection with sternal ulcers.

Kang, et al., (2018) conducted meta-analysis aimed to identify the effect of tight glycemic control (TGC) on mortality and morbidity among cardiac surgical patients. The final review included 26 studies with a total of 9,315 patients. Dense and liberal glycemic control did not vary in overall mortality. In addition, there was a reduced risk of sepsis, acute kidney damage, surgical infection, atrial fibrillation and an increased risk of hypoglycaemia and extreme hypoglycaemia associated with TGC. The study concluded that perioperative TGC (upper glucose target ≤150 mg/dL) was linked significantly with a reduction in short term mortality, cardiac surgical mortality, some postoperative complications and non-diabetic mortality compared to liberal regulation. Perioperative TGC can support patients when completed, despite the increased risk of hypoglycemic incidents.

Desai et al., (2012) conducted a study to test the hypothesis in which a liberal blood glucose strategy (121 to 180 mg/dL) is not worse than a strict blood glucose strategy (90 to 120 mg/dL) for outcomes in patients after CABG surgery. In this prospective randomized study, a total of 189 patients who had undergone coronary artery bypass grafting were recruited to compare two glucose management methods for periodic patient outcomes. The authors found that the groups corresponded preoperatively to hemoglobin Alc and the number of patients with diabetes. The liberal group proved to be worse than the severe perioperative complication and superior to the regulation of glucose and the management of target areas. There were slightly fewer patients with hypoglycaemic events in the liberal group (≤60 mg/dL; P-value ≤0.001). In summary, this research found that maintaining blood sugar after CABG in a liberal strategy led to comparable results compared to a strict target strategy and was superior in regulating and managing the target region. depend on the finding of this study, a target serum blood glucose range 121 - 180 mg/dL is recommended for patients following coronary artery bypass grafting suggested by the Society of Thoracic Surgeons.

Bláha, et al., (2015) conducted a randomized controlled trial that aimed to compare the effects of postoperative initiation of TGC versus initiation of TGC in perioperative on postoperative side effects in cardiac surgery patients. Participants included 2,383 hemodynamically healthy patients who underwent major cardiac surgery for at least two consecutive days with expected postoperative intensive care. Perioperatively or postoperatively, intensive insulin therapy with a target glucose range of 4.4 - 6.1 mmol/L has been initiated. The study results showed that despite only modest changes in glucose regulation, initiated of TGC in perioperative period significantly decrease of postoperative complications. No significant effect was seen in diabetic patients in perioperative (blood glucose) despite significantly improved glucose regulation. Non-diabetic patients were motivated by the positive effects of TGC on postoperative complications, whereas the study concluded that initiation of intensive insulin therapy in perioperative period in cardiac surgery decrease postoperative morbidity in non-diabetic patients.

Giakoumidakis et al., (2013) conducted a study to identify the effects of intensive glycemic control postoperative on outcomes of patients. A quasi-experimental design was assigned to a total of 212 patients with cardiac surgery: a therapy group (n=105) with a blood glucose target of 120-160 mg/dl or a control group (n=107) with targeted blood glucose levels of 161 to 200 mg/dl or. The two groups were compared with intubation time, length of stay, mortality, and the incidence of extreme hypoglycaemia and the frequency of postoperative infections. The results showed that the mean postoperative blood sugar levels relative to the control group were slightly lower for the treatment group (153.7 mg/dl vs. 173.7 mg /dl, P-value $\leq$0.001). Reduced mortality was closely correlated with intensive glycemic control (7 deaths / 105 control group patients compared with 1 death / 105 treatment group patients; p = 0.033). Regarding other patient effects, the authors found no statistically relevant compounds. The authors concluded that this quasi-experimental study showed lower morbidity with more intense regulation of blood glucose. The other patient outcomes observed were not affected by successful postoperative glycemic control.

Boreland et al. (2015) published a systematic analysis on strict glycemic control with continuous insulin infusion effects on SSIs and readmission of patients with DM after cardiac surgery to achieve serum blood sugar levels $\leq$200 mg/dL. Random and quasi-experimental experiments were included in a comprehensive systematic analysis. A meta analysis of 10 studies showed that continuous glycemic controlled insulin infusion to achieve blood sugar levels $\leq$ 200 mg/dL significantly decrease the patient's SSIs rates. The authors concluded that maintain blood glucose levels $\leq$ 200 mg/dL at all stages of the perioperative period with continuous insulin infusion will minimize the incidence of SSIs in cardiac surgery patients with diabetes.

A review of 1,100 diabetic patients underwent cardiac surgery between 2008 and 2009 was performed by Michaelian, et al., (2011). The data were collected from computerized documents and the graphs were analyzed to determine the reasons for rehospitalization. Primary outcome included the following: mean blood sugar during the intraoperative period and immediate postoperative, frequency of hypoglycaemia (defined as serum blood glucose, 70 mg/dl) and level of consciousness, rates of infection and recurrence before and after initiation of protocol. Subsequent glycemic control, before performing glycemic control values, was compared with baseline. Perioperative glycemic control was definitely improved by a procedure such as systematic preoperative preparation, monitoring and treatment of elevated blood sugar (BG). Preoperative mean BG decreased from 191 to 155 mg/dl (P = 0.016); agent BG decreased from 189 to 168 mg/dl (P = 0.094) postoperatively. The number of patients who preoperatively showed BG greater than 180 mg/dl and achieved BG less than 180 mg/dl increased from 21 percent to 43 percent (P = .09) postoperatively. From baseline to after implementation, the infection rate decreased from 12.4 percent to 8.8 percent. There was a trend towards improving the readmission rate. With the new protocol, data showed a trend towards change. It is possible to achieve strong perioperative glycemic regulation without increased risk of hypoglycemia.

A randomized control study conducted by Blaha, et al. (2006) compare in intensive care three insulin titration soft glycemic control (TGC) protocols: an absolute glucose protocol, a comparative glucose shift protocol and an improved predictive control model (eMPC) algorithm. Three protocols with a glycemic target range from 4.4 to 6.1 mmol /L were randomly assigned to a total of 120 consecutive patients after cardiac surgery. Intravenous insulin was administered continuously or in combination with insulin bolus (Matias protocol). Blood glucose was assessed at the request of the protocols at intervals of 1 to 4 hours. The results showed that eMPC algorithms delivered best. Compared with one in the Matias group and two in the Bath group, no significant hypoglycemic events (2.3 mmol /L) occurred in the eMPC group. The authors concluded that eMPC algorithms offer the best TGC without increasing the risk of extreme hypoglycemia and require at least glucose measurements. Overall, all procedures were successful in preserving TGC in patients undergoing cardiac surgery.

In Iran, Zadeh et al. (2016) conducted a study to compare the results of patients undergoing cardiac surgery through glucose regulation in two ways: tightly adjusted compared to traditional methods. It was a randomized open-label monitoring study of 75 diabetic patients who underwent open heart surgery. Patients were assigned to randomized (regular blood glucose levels maintained at 100-120 mg/dl) and traditional (blood glucose ≤200 mg/dl) frequent checks. Hospital death, wound infection, duration of mechanical ventilation, cardiac arrhythmias, cerebrovascular attack and acute renal failure were among the primary endpoints. The secondary endpoint was ICA's remaining duration. Complications after 30 days of surgery were reported. The results showed that there was no significant difference between the groups in patterns of changes in blood sugar during the operation and at the ICU. The result indicates a significant difference between blood glucose measurements at different periods (P-value≤0.001). In both groups, the incidence of hypoglycemia was low (one patient in each group and did not vary significantly between the two groups. In 34 patients with a modified close control group, hypokalemia was the most common adverse reaction compared with eight patients in the traditional one (P ≤0.001). was observed in a patient in the treatment group after 30 days, compared with 7 in the control group (P ≤0.05), which was significant. The authors concluded that the reduced incidence of hypoglycemia and hyperglycemic complications was associated with modified tight regulation of almost normal blood sugar levels during heart surgery.

Chapter Three

Materials and Methods

3.1 Design

A quasi-experimental design study conducted among diabetic patients undergoing CABG. One-centered clinical trial performed among male and female diabetic patients aged 18-70 years with ASA II-III undergoing CABG at AL-Ahli Hospital, Hebron-Palestine. Patients with cardiac surgery were assigned by a quasi-experimental design: a) a historical (control group (n = 50) received intermittent insulin with targeted blood glucose levels based on the slide scale in the hospital and an experimental group (n = 50) with glycemic control was maintained 150-180 mg/dl as the protocol used in the operating room. Intraoperative, the blood sugar was checked every 30 minutes before the patients were connected to the cardiopulmonary machine and every 15 minutes after they were connected to the cardiopulmonary machine until the end of the operation. At the ICU, blood sugar was checked every two hours until 48 hours after surgery. No subcutaneous insulin or oral antidiabetic drug was prescribed during this period. The protocol for insulin administration was discontinued after 48 hours after surgery. Patients turn to prescribed drugs or a subcutaneous insulin regimen using institutional guidelines before discontinuing intravenous insulin infusions based on patients’ needs.

3.2 Site and setting

The study was conducted at AL-Ahli Hospital, Hebron-Palestine, and Department of Cardiology.

3.3 Study period

Between October 2019 and June 2020 for experimental group (E) and between June 2018 and September 2019 for control group.

3.4 Sample size

is calculated using Pocock's sample size formula (ie Pocock's sample size formula) which can be used directly to compare the proportions P1 and P2 in two equal groups:

To determine the optimal sample size for a study that ensures a sufficient effect to detect statistical significance, computational power for the study at 80% and the level of alpha as p ≤0.05.

The following formula is used

$$n = \frac{(P_1(1-P_1) + P_2(1-P_2))}{(P_1-P_2)^2}(Z_{\alpha/2} + Z_{\beta})^2$$

Procedure of calculation

$$n = \frac{(P_1(1-P_1) + P_2(1-P_2))}{(P_1-P_2)^2}(Z_{\alpha/2} + Z_{\beta})^2$$

Where:

n: required sample size

P_1: estimated proportion of study outcome in the exposed group (i.e. combination therapy) (P_1 = 0.18).

P_2: estimated proportion of study outcome in the unexposed group (placebo therapy) (P_2 = 0.48).

α: level of statistical significance

$Z_{\alpha/2:}$ Represents the desired level of statistical significance (typically 1.96 for α = 0.05)

$Z_{\beta:}$ Represents the desired power (typically 0.84 for 80% power)

$$n = \frac{(0.18\ (1\text{-}0.18) + 0.48\ (1\text{-}0.48))\ (1.96+ 0.84)^2}{(0.18\text{-}0.48)^2}$$

$$n = \frac{(0.18\ (0.82) + 0.48\ (0.52))\ (2.8)^2}{(0.30)^2}$$

$$n = \underline{(0.14 + 0.24)}\ \ (7.84)0.09$$

$$n = \frac{(0.38)\ \ (7.84)}{0.09}$$

n ≈ 33 patients

Thus, a total of 66 patients (33 for each group) should be targeted for recruitment into the study. We were recruited 50 patients in each group, totally 100 patients to cover the drop out.

3.5 Inclusion criteria

1. Diabetic patients scheduled for CABG surgery

2. The ages between 18 and 70 years are included.

3. All patients diagnosed with DM undergoing first-time, non-acute CABG.

4. Patients with EC> 30%

5. Patients who started an insulin infusion while in the operating room.

6. Surgery that requires coronary bypass (CPB)

7. Patient's signed consent form to participate in the study.

3.6 Exclusion criteria

1. Patients with EC ≤30%.

2. Patients with ketoacidosis or hyperosmolar coma.

3. Repeat operation of CABG.

4. Patients diagnosed with cerebrovascular accident or transient ischemic attack.

5. History of liver disease.

6. Patients undergoing additional procedure with CABG (such as CABG with valve repair).

7. All non-diabetic patients undergoing CABG.

8. Renal impairment or renal failure (serum creatinine preoperative ≥ 1.5 mg/dl).

9. any other Mental or Neurological disorder.

10. patients diagnosed with Chronic obstructive pulmonary disease.

11. Emergency operations.

12. History of previous cardiac surgery.

13. patients who have Hemodynamic support during intraoperative period and / or during postoperative period in the first 24 hours with intra-aortic balloon pump.

3.7 Study treatment and intervention

We measured serum blood glucose level (baseline) in all included patients underwent CABG. Then, according on these baseline data, we started treatment by continuous infusion intravenously of Act rapid insulin (50 IU 50 ml 0.9% NaCl). Intraoperative glucose interventions and procedures are under the supervision of the anesthesiologists, whose aimed to maintain serum blood glucose level between 150 - 180 mg/dl intraoperatively and for the first 48 hours postoperatively. Intravenous insulin therapy started in the operating room at the time of induction. The care staff is not blind. Intraoperatively, the blood sugar was checked every 30 minutes before the patients were connected to the cardiopulmonary machine and every 15 minutes after they were connected to the cardiopulmonary machine until the end of the operation. At the CCU, In the CCU monitoring BG levels each houre during continuous insulin infusion until BG levels reach target range for 3 hours, then every 2 hours monitoring BG levels for the next 48 hours. monitoring of BG is performed using the same blood gas through patient's arterial line blood and then analyzed through Glucose Accu-Chek. For the experimental group, exclusively administration of insulin through continuous infusion intravenously using a volumetric infusion pump through a central venous catheter. Insulin infusion rate was controlled according target BG levels in this study protocol. Patients are managed intra-operatively with insulin drip (Michaelian, 2011) based on table (1) below. Adjusted the insulin infusion rate upon to the ordered regimen intraoperatively (table 1) and 48 hours postoperatively (Table 2).

Table 1. Patients are managed intra-operatively with insulin drip (Michaelian, 2011). Adjusted the insulin infusion rate upon to the ordered regimen.

Glucose level mg/dl	Regimen
Less than 70	Notify physician, discontinue drip and follow hypoglycemia guidelines
70-100	0 IU/hour
101-120	2.5 IU/hour
121-150	4.5 IU/hour
151-200	6 IU/hour
201-250	8 IU/hour
251-299	9 IU/hour
More than 300	Notify physician

Table 2. Patients are managed post-operatively with insulin drip (Michaelian, 2011). Adjusted the insulin infusion rate upon to the ordered regimen.

Blood glucose level mg/dl	Regimen
Less than 80	Notify physician, discontinue drip and follow hypoglycemia guideline
150-200	6 IU/hour
201-250	8 IU/hour
251-299	9 IU/hour

A historical control group - standardized care (C group) (n = 50).

Retrospective patient's data analysis was conducted. This group included patient's who underwent CABG between June 2018 and September 2019 at the same hospital, with the same surgical team, CCU staff and hospital infection control staff during both periods. As part of the criteria for inclusion / exclusion surgery, this was achieved by reviewing the hospital records of all patients with CABG who had received the same CCU care during the same period one year earlier to minimize the effects of seasonal variations on infection indications between the two groups. Information obtained from computerized medical records and examined charts.

Al-Ahli Hospital CCU protocol for diabetic patient undergoing cardiac surgery was applied at the historical group.

3.7.1 Pre-operative period

- Admit patient to intermediate CCU ward 48h before surgery.
- Random blood sugar (RBS q6h before surgery and give Simple insulin according.
- Patients undergoing CABG should be fasting 12h before surgery
- Stop all oral anti-diabetic.
- Take RBS during surgery q2h. If it is above 200mg/dl give insulin give simple insulin IV to keep blood glucose less than 200mg/dl.

3.7.2 Post-operative period

- RBS should be taken every hour for 2 hours.
- Then Q 4-6 hours and keep RBS below 200mg/dl.
- Insulin infusion should be started through pump machine if RBS more than 200mg/dl for more than two readings.

3.7.3 Data included the following in both groups:

1. Glycemic control during the preoperative, intraoperative and postoperative period up to 48 hours.

2. Presence of hypoglycemia (defined as BG ≤70 mg/dl).

3. Length of stay (LOS) at CCU and hospital, infection at surgical site, mortality in hospital and readmission rate

4. Additional complications such as urinary tract infection, pneumonia, stroke and others

3.8 Monitoring of Blood glucose and insulin treatment regimens.

BG is monitored according to the proposed rule in the protocol and insulin is administered accordingly. continuous infusion of Insulin (Act rapid HM) is given in a CVP line as a. A standard concentration of 50 IU = 0.5 ml Act rapid HM insulin in 49.5 ml 0.9% NaCl is used (1 international unit / 1 ml).

patients' clinical history data and Clinical parameters including gender, age, weight, height, body mass index, duration of surgery and anesthesia, duration of mechanical ventilation postoperatively recorded. Side effects are monitored and documented continuously. An experimental group (50) with a target BG postoperatively of 150-180 mg/dl for the first 48 hours.

3.8.1 Study Variables and measurement

The dependent variables for the current study (primary outcomes)

- Incidence of postoperative surgical infection (postoperative infections with clinical - laboratory evidence, microbiological documentation, pain or tenderness, redness or heat, purulent drainage, local swelling, sternal instability and leukocytosis).
- CCU and hospital length of stay (from surgery to discharge).
- Incidence of hypoglycemia (blood sugar levels ≤ 70 mg/dl).
- Early mortality (the death during hospital).

3.8.2 Validity of the data sheet

Content validity of this study ensured through the protocol was retrieved from previous review of Reddy, et al., (2014). We mimic previous studies as a validated improvement of the data sheet by inviting an expert panel (El Emam 2000; Dyba˚, 2000). We spoke to experts with different backgrounds recommended by Lauesen and Vinter (2001). Experts were recruited from a population of experienced practitioners and researchers in the areas of process improvement. These areas of competence are represented to ensure that the practitioner's needs and research knowledge during the early development are returned to the researcher's recommendations for experts who participate in a process assessment that supports this process. We define an expert in connection with this study as a person who is a researcher (b) has practical experience in the field for several years (Beecham, et al., 2005).

The validation of the data sheet was performed by involving 11 experts. This panel is a collection of individuals with demonstrated expertise in their profession with one intensivist, two cardiac surgeon, two anesthesiologists, three CCU nurses , two researchers and a statistician to get expert feedback to evaluate and support the development of data sheets. Examining components and filling in a detailed data sheet was performed (Beecham, et al., 2005). This is shown in the work of others carried out by Dyba˚ (2000) who used 11 experts to carry out their review process, the value of expert knowledge is also recognized in the evaluation which suggests methods for formally capturing expert assessment (Rosqvist et al., 2003). After current results of validation of data sheets. We linked results to the success criteria to get an impression of strengths and weaknesses. We modified the data sheet based on comments from the expert panel that gives confidence in its representation. The reliability of using expert assessment is shown in other work. For example, Lauesen and Vinter (2001) found that experts' ability to predict techniques to prevent requirements errors was very high when implemented.

3.8.3 Pilot test study

The purpose of conducting a pilot study is to investigate the feasibility of a strategy intended for use on a larger scale (Thabane et al., 2010, p. 1), A pilot research encourages decision-making and therefore functions as a "small-scale experiment or set of measures to determine how and whether to start a full-scale plan" (paragraph 1, Collins English Dictionary, 2014).

The alleged aim of the pilot studies was typically only to evaluate the measures outlined in a previously formulated study strategy on a small scale, and then changes would be made to the plan depending on the pilot's findings (Ackerman & Lohnes, 1981) and tested all techniques used for data collection. The specific pre-test of a particular research instrument which is a data sheet. In fact, the pilot includes a risk reduction strategy to reduce the risk of failure in a major project. Pilot testing in the current study was performed to test data collection sheets on five patients in the historical group and five patients in the experimental group. A pilot study was conducted to identify potential problem areas. Two observers filled in the data sheet in the historical group and five data sheets were applied to the patients in the experimental group to test and refine the study procedure, no changes were made in the data sheet, therefore data sheets were included in the large study.

3.8.4 Procedure

A) The patients enrolled in a protocol for tight glycemic control. After patient arrive to the OR, standard monitoring included, pulse oximetry and arterial line for continuous monitoring blood gases and arterial blood pressure and five-lead electrocardiography are used. After induction of general anesthesia, arterial line and CVP line are inserted, and baseline BG checked via an ACCU- check glucometer. If the BG level is ≥181 mg/dl, an infusion of 50 IU of act-rapid insulin in 49.5 ml

0.9 saline is started aimed was maintaining BG level between 150-180 mg/dl.

In all patients, blood glucose is regulated during the first 48 h post-operatively.

B) Participants underwent only clear liquid by mouth for the first 48 hours after surgery and have not received any subcutaneous insulin or diabetic medications. For all patients, caloric intake is similar.

C) Using the same blood gas analyzer, blood glucose tests are carried out by collecting a blood sample from an arterial line.

D) For the experimental group, insulin is administered exclusively through continuous infusion intravenously using volumetric infusion pumps via the CVP line. The rate of insulin infusions dependent on the intended levels of BG according to this study's insulin infusion protocol.

E) BG was tested every 30 minutes before the patients were attached to the cardiopulmonary machine and every 15 minutes after the patients were attached to the cardiopulmonary machine before the completion of surgery.

f) In the CCU, blood glucose levels are checked every hour during insulin therapy until blood glucose levels are within the 3-hour goal range and then every 2 hours.

G) The insulin administration protocols discontinued 48 hours after surgery, patients were subsequently weaned from the insulin drip and started on prior prescribed medication.

H) Adjust the infusion rate according to the above regimen. The insulin infusion protocol of the current study based on international literature.

(H. hypoglycemia), blood glucose less than 70 mg/dl that treated with 50 cc of dextrose 50%.

3.9 Data Collection

3.9.1 Pre-operative

Data sheet was used that includes Patients' demographic data (age, gender, weight, height, and body mass index), Preoperative serum glucose levels, duration of surgery, anesthesia duration, history of hypertension, history of DM, history of arrhythmias, history of myocardial infarction, history of atrial fibrillation, history of smoking, HbA1c,.

3.9.2 Intraoperative

Initiation of the intravenous insulin infusion at a BG threshold no greater than 180 mg/dL for the treatment of persistent hyperglycemia in critically ill patients with a target blood glucose of 150-180 mg/dL.

BG level checked every 30 min intraoperatively.

BG level checked every 15 min In the case of cardioplegia, cooling and rewarming.

The patient hypoglycemia considered if BG is $\leq$ 70 mg/dl.

The patient severe hypoglycemia considered if BG $\leq$ 50 mg/dl.

3.9.3 Postoperative

During insulin therapy, BG levels are monitored every 1 hour until blood glucose levels are below the target range for 3 hours, then levels are monitored every 2 hours. When levels are out of the target range, hourly BG monitoring is resumed. Sternal wound infection, ICU-LOS (days), Postoperative hospital LOS (days), readmission, In-hospital mortality recorded. The study terminated when the patient is discharged from the hospital.

3.9.4 Statistical Methods

Statistical package for social sciences (SPSS) Version 25 is used for data analysis. Descriptive statistics (frequencies and percentages, Means, Standard Deviations) are used. The following tests and Methods are used to analyze the results where the P-Value $\leq$ 0.05 is considered significant:

Chi-Square test: tests the differences between groups of patients for qualitative variables such as: Gender, History of MI, History of arrhythmia, History of atrial fibrillation, History of smoking, Sternal wound infection, Urinary tract infection, Superficial sternal infection, Hypoglycemia, Urinary tract infection, Pneumonia, Readmission, In-hospital mortality, Cardiac complication, Stroke, Acute renal failure, Hypokalemia, Deep sternal infection.

Two Independent Samples T test : tests the differences between groups of patients for quantitative variables such as : Age, Weight, High, BMI, Ejection Fraction, Preoperative Blood Glucose, Duration of surgery, Duration of Anesthesia, Postoperative Blood Glucose, Hemoglobin A1c, Intra-Operative Blood Glucose Measurements, Post-Operative Blood Glucose Measurements, ICU-LOS(days), Postoperative hospital LOS (days).

3.9.5 Ethical Consideration

Prior to being enrolled for the study, written informed consent was received from all participants. The study was accepted by the An-Najah National University Institutional Review Board and the Al-Ahli Hospital Ethics Review Committee. Each possible topic was told by the same researchers about the aims, procedures, anticipated advantages, and potential risks of the preoperative analysis. The survey was conducted in compliance with the ethical principles of the Human Experimentation Responsible Institutional Committee and with the Helsinki Declaration of 1975, which was amended in 2008. Precautions have been taken to preserve researchers' credibility and the security of their sensitive records. This involves restricting the quantity of personal information to the very minimum, giving each subject an identification number and connecting the identification number to the actual analysis information, removing subject names as soon as the data is processed, and storing all identifying information and identification number lists in a safe and locked file. There is no section of routine treatment excluded.

Chapter Four

The Results

This clinical study comprised 100 diabetic patients who underwent open cardiac surgery, and were divided into historical and experiment groups: fifty patients in each group.

Table 3. Means, Standard deviations and Independent Samples T-test results for differences between the Historical and Experimental groups in demographic Data.

Demographic Data	**Historical N(%)**	**Experimental N(%)**	**Chi-square**	**P-value**
Gender: Male	45(90%)	41(82%)	1.329	0.249
Female	5(10%)	9(18%)		
Demographic Data	Historical (N=50) Mean±S.D	Experimental (N=50) Mean±S.D	t	P-Value
Age	56.76±8.33	56.38±6.45	0.255	0.799
Weight	85.44±12.85	86.9±11.32	-0.603	0.548
Hight	170.22±8.67	170.32±9.06	-0.056	0.955
BMI	29.97±4.22	30.51±5.63	-0.550	0.584

The results in the table (3) above showed that there are no significant differences between the Historical group and the Experimental group in Gender, Age, Weight, High, and BMI (P-values>0.05).

Table 4. Means, Standard deviations and Independent Samples T-test results for differences between the Historical and Experimental groups in some indicators.*

Demographic Data	Historical (N=50) Mean±S.D	Experimental (N=50) Mean±S.D	t	P-Value
Ejection Fraction %	52.44±5.82	50.68±5.88	1.486	0.141
Preoperative Blood Glucose	185.22±38.76	173.72±18.74	1.889	0.063
Duration of surgery	5.12±0.33	5.1±0.3	0.317	0.752
Duration of Anesthesia	4.19±0.36	4.08±0.27	1.711	0.090
Hemoglobin A1c	9.12±1	9.71±0.91	-3.103	0.003**

*** T-test results adjusted for un-equality of variances.**
****Significant at 0.05 level.**

The results in the table (4) above show that there are significant differences between the historical group and the experimental group in Hemoglobin A1c (P-values ≤0.05).The results exhibited that the mean of Hemoglobin A1c in the Historical group (mean=9.12) is significantly lower than that in the Experimental group (mean=9.71) (Table 4).

From the other hand, the results showed that there are no significant differences between the historical group and the experimental group in ejection fraction, preoperative blood glucose, duration of surgery, and duration of Anesthesia (P-values>0.05).

Table 5. Frequencies, Percentages and Chi-square test results for differences between the Historical and the Experimental groups in some indicators.

Demographic Data	Historical N (%)	Experimental N (%)	Chi-square	P-value
History of MI	0(0%)	4(8%)	3.922	0.048*
History of arrhythmia	0(0%)	0(0%)	----	----
History of atrial fibrillation	1(2.1%)	0(0%)	1.052	0.305
History of smoking	16(33.3%)	14(28%)	0.328	0.567

***Significant at 0.05 level.**

The results in the table (5) above show that there are significant differences between the Historical group and the Experimental group only in the History of MI (P-value≤0.05). The results exhibited that the number of patients who had History of MI in the Historical group(N(%)=0(0%)) is significantly lower than that in the Experimental group(N(%)=4(8%)).

From the other hand, the results showed that there are **no** significant differences between the Historical group and the Experimental group in History of arrhythmia, History of atrial fibrillation, and in History of smoking(P-values>0.05).

Table 6. Means, Standard deviations and Independent Samples T-test results for differences between the Historical and Experimental groups in Intra-Operative and Post-Operative Blood Glucose Measurements.*

Blood Glucose Measurements	Historical(N=50) Mean±S.D	Experimental(N=50) Mean±S.D	t	P-Value
Intra-Operative BGM	223.03±47.32	170.91±2.64	7.776	0.000**
Post-Operative BGM	283.08±74.96	168.88±16.22	10.529	0.000**

***T-test results adjusted for un-equality of variances.**

****Significant at 0.05 level.**

The results in the table (6) above show that there are significant differences in the Intra-Operative Blood Glucose Measurement between the Historical group and the Experimental group(P-value=0.000≤0.05). The results exhibited that Intra-Operative Blood Glucose Measurement in the Historical group (mean=223.03) is significantly higher than that in the Experimental group (mean=170.91).

The results in the table (6) above show that there are significant differences in the post-Operative Blood Glucose Measurement between the Historical group and the Experimental group (P-value=0.000≤0.05). The results exhibited that post-Operative Blood Glucose Measurement in the Historical group (mean=283.08) is significantly higher than that in the Experimental group (mean=168.88).

Table 7. Frequencies, Percentages and Chi-square test results for differences between the Historical and the Experimental groups in Blood Glucose Measurements.

Blood Glucose Measurements	Level	Historical N(%)	Experimental N(%)	Chi-square	P-value
Intra-Operative BGM	≤=180	9(18%)	49(98%)	65.681	0.000
	>180	41(82%)	1(2%)		
Post-Operative BGM	<=180	28(56%)	50(100%)	28.205	0.000
	>180	22(44%)	0(0%)		

***Significant at 0.05 level.**

The results in the table (7) above show that there are significant differences between the Historical group and the Experimental group only in percentages of patients presenting with a blood glucose level greater than

180 mg/dL Intra-Operative and Post-Operative (P-values<0.05). The results exhibited that regarding Intra-Operative, only 1(2%) patients in Experimental group presenting with a blood glucose level greater than 180 mg/dL while 41(82%) patients in Historical group presenting with a blood glucose level greater than 180 mg/dL.

Regarding Post-Operative, no patients in Experimental group presenting with a blood glucose level greater than 180 mg/dL while22(44%) patients in Historical group presenting with a blood glucose level greater than 180 mg/dL (Table 7).

Table 8. Frequencies, Percentages and Chi-square test results for differences between the Historical and the Experimental groups in Outcomes Measures.

Outcomes Measures	Historical N(%)	Experimental N(%)	Chi-square	P-value
Superficial sternal infection	3(6%)	0(0%)	3.093	0.079
Deep sternal infection	4(8%)	0(0%)	4.167	0.041*
Urinary tract infection	1(2%)	0(0%)	1.010	0.315
Pneumonia	4(8%)	0(0%)	4.167	0.041*
Readmission	1(2%)	0(0%)	1.010	0.315
In-hospital mortality	0(0%)	0(0%)	----	----
Cardiac complication	4(8%)	1(2%)	1.895	0.169
Stroke	4(8.2%)	0(0%)	4.253	0.039*
Acute renal failure	0(0%)	0(0%)	----	----
Hypoglycemia	5(10.2%)	2(4%)	1.450	0.229

***Significant at 0.05 level.**

The results in the table (8) above show that there are significant differences between the Historical group and the Experimental grouponly in Deep sternal infection, Pneumonia, Stroke (P-values<0.05). The results exhibited that the number of patients who haddeep sternal infectionin the Historical group(N(%)=4(8%)) is significantly higher than that in the Experimental group(N(%) p=0(0%)).

Also the results exhibited that the number of patients who hadPneumoniain the Historical group (N(%)=4(8%)) is significantly higher than that in the Experimental group (N(%)=0(0%)).

Also the results exhibited that the number of patients who hadStroke in the Historical group (N(%)=4(8.2%)) is significantly higher than that in the Experimental group (N(%)=0(0%)).

From the other hand, the results showed that there are nosignificant differences between the Historical group and the Experimental groupin Superficial sternal infection, Urinary tract infection, Readmission, In-hospital mortality, Cardiac complication, Acute renal failure, andHypoglycemia (P-values>0.05).

Table9. Means, Standard deviations and Independent Samples T-test results for differences between the Historical and Experimentalgroups in ICU-LOS and in Postoperative hospital LOS.*

Outcomes Measures	Historical (N=50) Mean±S.D	Experimental (N=50) Mean±S.D	t	P-Value
ICU-LOS(days)	4.14±0.9	2.18±0.39	14.091	0.000**
Postoperative hospital LOS(days)	5.72±0.86	4.98±0.71	4.687	0.000**

***T-test results adjusted for un-equality of variances.**

****Significant at 0.05 level.**

The results in the table above show that there are significant differences between the Historical group and the Experimental group in the ICU-LOS and in Postoperative hospital LOS(P-values = $0.000 \leq 0.05$). The results exhibited that the mean of ICU-LOS (days) in the Historical group (mean=4.14) is significantly higher than that in the Experimental group (mean=2.18). Also, the results exhibited that the mean of Postoperative hospital LOS (days) in the Historical group (mean=5.72) is significantly higher than that inthe Experimental group (mean=4.98).

Chapter Five
The Discussion

In this chapter discussion of the study's main findings. The outcomes of this research are correlated and contrasted with the results of the related existing literature. Clinical guidelines for future study and recommendations are established.

Diabetes Meletus is a Growing concern in public health and is also highly reverent to surgical patients as well. However, surgical results are adversely affected by both diagnosed and undiagnosed DM. The main aim of the perioperative duration of this group of patients is to avoid hyperglycemia. For this reason, risk stratification and medical optimization were recommended in the preoperative period; intravenous insulin and regular glycemic control with correction action of hyperglycemia were recommended in the intraoperative period to maintain glycemic targets of 150-180 mg/dl; and early return to oral feeding and initial therapy in the postoperative period.

The current comparative study was to evaluate the efficacy of tight glycemic Interventions for monitoring intraoperative and postoperative with a continuous insulin infusion to maintain blood glucose levels of 150-180 mg/dl to reduce the complications of open heart surgery. We used insulin for modified tight glucose control through a designed protocol to maintain BS in a range of 150-180 mg/dl in Tight Glucose Control (TGC).

It is predicted that blood glucose management during perioperative period and insulin administration in DM patients during open heart surgery would have benefit’s on outcome for DM patients. Insulin administration can lower free fatty acids, increase myocyte glucose uptake, and promote glycogenesis, protecting the heart from ischemia caused by cardiopulmonary bypass. (Girish, et al., 2014). Hyperglycemia may also have a pro-inflammatory effect, leading to postoperative platelet dysfunction, capillary leakage syndrome, and a weakened immune response, both of which can be avoided with proper glycemic regulation. (Stamou, et al., 2011).

Many studies shown that during the perioperative period strict glycemic control is linked with lower infection rates in DM patients have, reduced residence time (LOS) and faster recovery (Lazar, et al 2004; Furnary, et al 2007; Lecomte, et al 2008; Scalea , et al 2007). Perioperatively, control of DM is difficult to achieve due to the risk of hypoglycemia. Despite guidelines published on administration of insulin during the perioperative there is still great variation (Bilotta, et al. 2007; Gliste, et al. 2003; Rehman, et al. 2003).

5.1 Hyperglycemia

In the current study, there is a significant difference in the historical group between perioperative blood glucose M (SD) 185.22 ± 38.76 and postoperative blood glucose 283.08 ± 74.96 ($P \leq 0.0001$), the results indicate that patients in the historical group had significantly higher BG postoperatively than preoperatively. When we looked at the difference in the experimental group between preoperative BG M (SD) 173.72 ± 18.74 compared to postoperative BG 168.88 ± 16.22 (P = 0.1445), the results indicate that there was no difference between the two periods and that it was within the normal range of the Protocol. Preoperative BG improved from (M) 173 mg/dl before protocol implementation to 168 mg/dl.

Intraoperative, The number of patients 41 (82%) with ≥ 180 mg/dl in the historical group is significantly higher than the number of patients 1 (2%) in the experimental group. Absolute risk reduction: 80% of patients not have side effects during new treatment. 95% confidence interval: [68.67%, 91.33%]. Number needed to treat: You must treat 1.2 patients with new therapy to prevent a side effect that would have occurred under control. Postoperatively, the number of patients 22 (44%) with ≥ 180 mg/dl in the historical group is significantly higher than the number of patients 0 (0%) in the experimental group.

Absolute risk reduction: After the latest procedure, 44.00 percent of patients would not suffer side effects that they previously had under control. The 95% confidence interval is: [30.11%, 57.89%]

Number needed to treat: You must treat **2.3** patients with New Therapy to prevent 1 adverse event that would have happened under Control. 95% confidence interval: [1.7, 3.3].

hyperglycemia are well known from CABG exposure (Mills, et al 1973). The capacity of hyperglycemia, especially surgical or sternal wound infections, to disrupt leukocyte function by impaired phagocytosis and bactericidal function and lead to infection was not well known until later (Bagdade, 1974).

Acute hyperglycemia is known to have many adverse effects, including increased expression of leukocyte, decreased complement function, decreased vasodilation, endothelial adhesion molecules, increased cytokine levels, decreased Impaired neutrophil chemotaxis and phagocytosis due to reactive endothelial nitric oxide production (Lipshutz, et al., 2009). Leads to increased inflammation, vulnerability to infection and multiorgan dysfunction (Lipshutz, et al., 2009) and consequently, researchers can interpret the association between hyperglycemia and increased mortality in heart surgery.

Asida, et al distributed 100 people with diabetes into two classes of TGCs, and a common form of careful blood glucose control persisted from the onset of anesthesia to full patient stabilization and extubation. In the control group, the increase in serum sugar continued until the completion of the procedure (with a mean value of 227 mg/dl). The mean level of glucose in both groups were identical prior to CPB beginning. However, from the start of CPB to extubation, substantial variations were noticed between the two groups (Asida, et al 2013).

This consistent with previous studies in which the The combination of an increased prevalence and a poor perioperative response to diabetes has resulted in an increased rate of surgical complications, mortality and the cost of treatment (du Toit, et al., 2018). Perioperative glycemic control is widely reported to help minimize morbidity and mortality. In particular, blood glucose levels of ≤ 180 mg/dl are typically associated with a lower risk of adverse surgical results (Monteiro, et al., 2019). Several studies have also shown that the risk of complications is linked to hyperglycemia severity (Kotagal, et al., 2015). Abdelmalak et al. (2014) found that mortality in the first year is associated with preoperative glycemia (P-value <0.001). Frisch et al. (2010) have concluded that the probability of mortality rises in relation to the amount of perioperative glucose (P-value = 0.008) and that hyperglycemia is associated with a rise in hospital duration of stay (P-value = 0.001), a higher number of cases of infection (P-value =0.001), acute renal failure and acute myocardial infarction (P-value =0.005). McConnell, et al. (2019) also concluded that a higher proportion of surgical site infections are associated with postoperative hyperglycemia. Kotagal more recently. There was also a dose-response association between glycemic levels and compound adverse effects by et al (2015). Kwon, et al. (2013) established a dose-effect relationship between the effectiveness of insulin glycemic control and prognosis, and concluded that important objectives are perioperative measurement of glycemia and insulin administration.

5.2 HbA1c

In addition, the association between high preoperative HbA1c values and surgical outcomes has also been shown in several studies. A recent research by Narayan et al. (2017) found that in patients undergoing coronary bypass, HbA1c was linked to a higher risk of deep sternal wound infection (P=0.04) and respiratory problems (P=0.04). (P-value =0.01) by 6.5 percent. Similar findings were also made by Kallio, et al. (2015), showing a rise in the incidence of complications and a prolongation of hospitalization in uncontrolled HbA1c patients (P-value ≤0.001). Postoperative glycemic instability, a rise in significant adverse effects and a decline in intraoperative insulin sensitivity was also correlated with preoperative HbA1c values of 6.5 percent in other studies (Sato, et al., 2010). Glycemic regulation has thus been increasingly recognized as a perioperative target (Meneghini, et al., 2009), and when the value of glycemia and HbA1c is very high, it is advisable to postpone elective surgery (Oakley & Emond, 2011).

5.3 Hypoglycemia

In the current study, 5 (10.2%) patients with hypoglycemia were in the historical group and 2 (4%) in the control group (p = 0.229). The difference was not statistically significant. Further clinical tests to determine the benefits of strict regulation of blood glucose have demonstrated a detrimental effect on mortality due to hypoglycaemia and add to the research that contradicts the need for strict control of blood glucose (NICE-SUGAR Study Investigators, 2009).

In a quasi-experimental study conducted by Giakoumidakis, et al (2013) for 212 patients underwent cardiac surgery divided into two groups: a) 107 patients targeted blood glucose levels 160-200 mg/dl in a control group and b) 105 patients with blood glucose targets 121-159 mg/dl in therapy group. The study compared the two groups in terms of their intubation time, frequency of postoperative infections, they looked at death, duration of stay, and the rate of serious hypoglycemia, and found that neither of the participants had hypoglycemic incidents. This outcome highlights the safety of the process for insulin infusion. The efficacy of the insulin infusion regimen is shown by the slightly lower levels of blood sugar in the intensive insulin therapy group relative to the control group.

5.4 Sternal wound infection

Many glucose metabolism-related improvements are correlated with the perioperative period. Counter-regulatory hormones are rising, leading to increased gluconeogenesis, such as adrenaline, cortisol and glucagon. Previous conditions also influence patients to develop hyperglycemia in conjunction with elevated insulin tolerance and reduced insulin production.

Perioperative hyperglycemia is related to depressed bactericidal ability, delayed chemotaxis, reduced phagocytosis, and granulocyte adhesion defects (Hanazaki, et al 2009). The level of hyperglycemia, which has been shown to inhibit phagocytic function and thus increase infection susceptibility, is as low as 200 mg/dL (MacRury, et al. 1998). Surgical diseases, including multi-organ failure and increased mortality, have severe implications (Hanazaki, et al 2009; MacRury, et al 1998). By inhibiting the tissue factor, plasminogen activator inhibitor-1, and the intranuclear factor kB, insulin has a potent and acute anti-inflammatory effect. Insulin has a significant function to play, not only in blood sugar control but also as an anti-inflammatory and antioxidant agent (Hanazaki, et al 2009).

In the current study, there were 4 (8%) patients in the historical group with deep sternal infection compared to 0 (0%) in the close blood glucose control group, the difference was significant between the groups in favor of strict blood glucose control ($p = 0.041$). Absolute risk reduction of sternal wound infection: 8% of participants not experienced any side effect during New Therapy that they would have under control.

Number needed to treat: You must treat 12.5 patients with close blood glucose control therapy to prevent 1 side effect (deep stern infection) that would have occurred under control.

This result is in alignment with Study has tested the effects of blood glucose control in diabetic patients undergoing open heart surgery for the prevention of sternal wound infection (Zerr, et al 1997). A research by Zerr, et al compared an insulin infusion regimen with natural blood glucose regulation to sustain postoperative blood glucose ≤200 mg/dL (Zerr, et al 1997). The study included 1585 diabetic patients: 990 patients from 1987 to 1991 before the insulin infusion procedure and 595 patients from 1991 to 1993 after the implementation of the protocol. Compared with 206 mg/dL in the monitoring group, the average blood glucose value in the protocol group was 172 mg/dL. The average blood glucose was 176 mg/dL in the protocol group and 195 mg/dL in the monitoring group on postoperative day two. The frequency of deep wound infections, including both the sternal site and leg incision, declined from 2.4% in the control group to 1.5% in the treatment group ($P \leq 0.02$); the concentrations were 2.8% and 0.74% respectively for the sternal site alone.

In the current study the M(SD) postoperative blood glucose value in historical group was 283.08±74.96 compared with 168.88±16.22 in the tight blood glucose group (p=0.000). There were 4(8%) patients in historical group with deep sternal infection compared with 0(0%) patients in the tight blood glucose group (p=0.041).This result is in agreement with the study results conducted by Zerr, et al showed that Increased average serum glucose were shown to be associated with deep sternal bacterial infection during the first 48 hours of surgery and to be an independent predictive factor for the occurrence of deep sternal infection (Zerr, et al 1997).

The current study results are consistent with the A follow-up analysis results conducted by Furnary, et al, (2015) examining deep sternal SSI in patients with diabetes following heart surgery; sliding insulin was given every 4 hours by the standard group to stabilize blood glucose ≤ 200 mg/dL, and a constant insulin infusion were given to maintain blood sugar levels ≤ 200 mg/dL. (Furnary, et al. 1999). In the analysis (P = 0.005), the researchers observed a substantial decline in deep sternal infections. Also, our results were completed in an ornament with the latest NICE-SUGAR study, and the results suggest that intensive glucose control in this large international randomized study Increased mortality at the Intensive care unit for adults. The investigation revealed that a blood glucose level of less than 180 mg/dl was an acceptable level to be achieved (The NICE-SUGAR Study Investigators, 2009). In our study 41(82%) patients in the historical group had BG >180 intraoperative compared with 1(2%) patient in the hight blood glucose group (p=0.000) and 22(44%) patient had BG >180 postoperative compared with 0(0%) postoperative (=0.000).

Another research assessing the results of strict BG regulation, from 120 - 200 mg/dL, with consistent infusion of insulin in DM patients after cardiac surgery noted decrease duration of hospital stay and deep SSIs, but there weren’t substantial variations between them (Vora, et al 2004). Study of Carr, et al (2005) assessing the effect of lower BG targets (≤130 mg/dL) revealed a substantial advantage of intensive BG regulation in patient’s outcome, but patients mortality was not identified. The research involved both diabetic and non-diabetic patients with a continuous insulin infusion initiated over defined periods of time with declining blood glucose intervals. Insulin infusions were initiated during the last two phases of the study when blood glucose levels were >125 mg/dl and 110 mg/dl. The glucose levels of the patient were deemed to be well regulated for more than 50 percent of the time if they were ≤130 mg/dl. A drop in the frequency of sternal wound infection observers (0.4 to 0 percent) when blood glucose > 125 mg/dl was initiated with the insulin infusion. In the last step of the study, the same level of sternal wound infections was sustained when the insulin infusion was started at blood sugar > 110 mg/dl. (Carr, et al 2005).

High blood sugar levels in association with sternal wound infection during the first 48 hours following surgery (Zerr, et al 1997). Continuous follow-up (after a month) revealed statistically important findings for one patient with sternal infection in MTG and seven cases in CGC. It was also shown in a report by Hruska et al (2005). Continuous insulin infusion to sustain BS = 120-160 mg/dl has been shown to substantially reduce the degree of sternal SSIs in DM patients underwent CABG.

In the research by Zerr, et al. (1997), 1585 diabetes patients were split into management and protocol classes. Compared to 195 mg/dl in the control group, the mean BS of the protocol group was maintained at an average of 175 mg/dl. In both sternal and foot ulcers, the rate of wound inflammation declined from 2.4 percent in the control group to 1.5 percent in the treatment group. In the monitoring group, the rate of sternal infections was just 2.8 percent, compared with 0.74 percent in the care group. Elevated blood sugar levels association with sternal wound infection during the first 48 hours following surgery. One patient with sternal infection in MTGC and seven patients in CGC reported statistically important findings in long-term follow-up (after one month). The research was similarly performed by Hruska, Smith et al (2005). Furnary, et al (1999); Kramer, et al (1999) found close findings (2008). Although the incidence of sternal ulcer infection decreased in the TGC system in diabetic patients in their center who underwent open heart surgery, they found (from 2.6 percent before the start of the TGC method to 1 percent after the TGC method).

5.5 Mortality

In the current study, the mortality was zero in both groups so there was no significant difference between the groups regarding mortality.

However, other studies do not provide clear evidence of the association between inadequate regulation of postoperative blood sugar and increased mortality (Gandhi, et al., 2007; Lazar, et al., 2004; Groban, et al., 2002; Chan, et al., 2009). It is actually surprising because, relative to the traditional population, Gandhi et al (2007) observed a statistically substantial rise in the rate of death in the intensive insulin therapy community. In comparison, controlled trials (Wiener, et al., 2008; Griesdale, et al., 2009; Friedrich, et al., 2010) of a substantial number of chronically ill patients with psychiatric or surgical conditions have been used in three large meta-analyses, indicating that intensive insulin therapy has no effect on mortality.

A number of studies with prospective design (Furnary, et al 2003; Jones, et al 2003) or retrospective (Schmeltz, et al 2007; Lecomte, et al 2008) showed significantly higher Probability of mortality for postoperative hyperglycemia in DM patients underwent cardiac surgery.

However, In addition to the results of our study, Imran, et al. (2010) in their prospective retrospective analysis of 2856 cardiac surgery patients. there was no relationship between elevated BG levels and hospital mortality. According to the research conducted by Via et al. (2010), in cardiac surgery patients who developed a chronic critical disease, effective glycemic control during ICU ingestion and the first 12 hours postoperatively was associated with a higher risk of mortality relative to patients who developed a chronic critical disease and had poorer glycemic control during the same time.

Furnary, et al. (2008) assessed Hospital mortality of DM patients underwent CABG, participants received an insulin infusion to preserve BG for 72 hours following surgery and those in the control group received SC insulin to maintain BG. Throughout the study, BG targets were steadily reduced: the target was (group 1: 150 to 200 mg/dL) (group 2: 125 to 175 mg/dL) (group 3: 100 to 150 mg/dL). The mortality rate was 2.5 percent in the experiment groups, compared with 5.3 percent in the control group (P-Value ≤0.001). Within each interval, BG levels decreased steadily to allow nurses to grow familiar with the procedure and to ensure patient safety. In the insulin infusion community, overall mortality decreased, but it was uncertain if mortality decreased with each incremental decline in blood glucose targets.

Important advantages were provided by one study testing intensive BG regulation, BG 80 - 110 mg/dl. van den Berghe, et al. conducted the experiment. This randomized study included nearly 1,500 critically ill patients, consisting of both non-diabetic and DM patients underwent cardiac surgery. To control blood sugar at two separate ranges, a constant insulin injection was used 80 - 110 mg/dL in the intensive care unit and 180 - 200 mg/dL in the conventional group. The mean blood sugar levels were 143 and 173 mg/dl in the intensive and traditional care groups, respectively. In addition to decreases in the rate of septicemia, the number of blood transfusions, the duration of stay in the intensive care unit (ICU), the incidence of kidney failure, the number of blood diseases and other morbidities, there was a substantial decrease in overall mortality in the intensive care unit (4.6 percent) relative to the traditional group (8 percent) (P $\leq$0.04). (van den Berghe, et al 2001). This research demonstrated the greatest impact on mortality and led to additional experiments of cardiac surgery patients testing multiple blood glucose targets; however, none was able to replicate such a noticeable impact on patient outcomes.

Our study is not in line with the study conducted by Ingles et al, (2006).

In its randomized clinical study of 970 patients with heart surgery, good postoperative glucose regulation was found to have a clear association with lower early mortality (mortality in hospital and/or ICU). Moreover, we do not accept that the report uses meta-analysis of seven randomized controlled trials, Haga, et al (2011) concluded that the rate of early mortality was decreased by almost 50 percent by strict glycemic regulation. Vandenberg et al (2001) recorded that a drop in blood sugar by 50 mg/dl contributed to a 34 percent decrease in ICU mortality.

5.6 Length of stay

In the current study, the results show that there were significant differences between the historical group and the experimental group in ICU-LOS and in postoperative hospital LOS (P-values = 0.000 $\leq$0.05). The results showed that the mean value of ICU-LOS (days) in the historical group (mean = 4.14) is significantly higher than in the experimental group (mean = 2.18). The results also showed that the mean value of postoperative hospital LOS (days) in the historical group (mean = 5.72) is significantly higher than in the experimental group (mean = 4.98). Our results are inconsistent with the study results conducted by Chan, et al (2009) Evaluated reference levels for blood glucose: the treated range is 80 to 130 mg/dL and the control category is 160 to 200 mg/dL (Chan, et al. 2009). In various health results, including survival, duration of stay and frequency of infection, no distinction was found between the two groups.

The results of our study are also not contestants with Gandhi et al., (2007). Our results are in contrast to Haga et al (2011) It was found that the duration of MV and the length of hospital stay in the intensive care unit were greatly decreased in patients with effective glucose regulation. Furthermore, their is significant relationship between perioperative hyperglycemia and its effects, such as long-period ICU stay and overall hospital length of stay, was documented by Lazar et al (2004). Contrary to the findings of this report, several studies have found substantial evidence to link inadequate postoperative glycemic regulation with prolonged hospital stays in cardiac surgery patients (Jones, et al., 2008; Via, et al. 2010) and higher frequency of infections (Jones, et al., 2008; Via, et al. 2010) (Schmelz, et. al 2007; Lecomt, et al 2008).

5.7 Stroke

In the current study, there was a significant difference regarding the incidence of stroke, there were 4 (8.2%) patients who had stroke in the historical group and 0 (0%) in the dense blood sugar group. The results of the current study are consistent with the results of studies performed by Gandhi et al (2004) Compared to traditional therapy with insulin infusion (blood glucose target, 150-200 mg/dl) in both diabetic and non-diabetic patients, assessment of intensive blood glucose regulation with insulin infusion (target blood glucose, 80-100 mg/dl) Sternal wound diseases, excessive pulmonary breathing, heart arrhythmias, stroke, and acute renal impairment were assessed as cumulative outcomes of death within 30 days. Mean blood glucose in the intensive care and traditional groups was 123 versus 148 mg/dL during bypass and 114 versus 157 mg/dL postoperatively in the ICU, respectively. In the primary composite result, there was no substantial difference between the groups. Individual endpoints were analyzed independently and found a rise in deaths, strokes and heart blocks in the intensive insulin regulation group that involved pacemakers.

5.8 Recommended range of BG level ≤ 180 and 140 to 180 mg/dL.

In the current study, patients with diabetic underwent heart surgery continued on an insulin infusion protocol with a BG target of (150-180 mg/dl) in the experimental group, which is roughly in line with other previous studies to avoid hypoglycemia. Desai et al, (2012) showed that Liberal BG control (121to180 mg/dl) in patients with CAD was associated with less hypoglycemia. Lazar et al, (2011) In patients with diabetic heart surgery sustained on an insulin infusion regimen with a BG target of 120-180 mg/dL compared to 90-120 mg/dL, it was found that less episodes of hypoglycemia and no substantial variations in side effects were recorded. In a retrospective study of 4658 patients undergoing cardiac surgery, Bhamidipati et al (2011) observed that mild glycemic control (127-179 mg/dL) was higher than near glycemic control (≤126 mg/dL) with decreased morbidity and mortality and in patients with documented diabetes or perioperative hyperglycemia.

Based on the latest information, the new guidelines for the Society of Breast Surgeons and the AACE / ADA Consensus Statement appear to be appropriate and alleviate concerns about hypoglycaemia with the new recommended range ≤180 and 140 to 180 mg/dl. In order to further suggest an intense blood glucose target range of 80 to 110 mg/dl, especially in the cardiac surgery community, further research evaluating blood glucose target ranges seem appropriate. The average blood sugar in patients in the intensive care unit was around 140 mg/dl even after the Van Den Berghe trials (2001). Thus, it seems appropriate to test for blood sugar levels of about 140 mg/dL. Mortality and morbidity gains are seen with total hyperglycemia control; but, as previously assumed, the precise spectrum is not yet well established. In postoperative cardiac patients, further comparisons of particular glucose regions will allow a better understanding of the prescribed blood glucose targets, resulting in the best outcomes and the least occurrence of hypoglycemia.

The results of the current primary outcomes research are consistent with those of Gandhi (2007). 400 diabetic and non-diabetic patients, split into two categories, were analyzed in the TGC community with a BS range of 80-100 mg/dl. Mean BS was smaller in the care group at the end of the procedure than in the control group (114 mg/dl relative to 157 mg/dl). One of these complications resulted in 44% of the patients in the treatment group and 46% of the patients in the control group: mortality (4 to 0), stroke (8 to 1), and a mean ICU stay of 2 days in both categories. Postoperative mortality and morbidity did not decrease despite the ongoing insulin infusion at the ICU (Gandhi, et al. 2007).

Currently, STS has recommended that heart surgery patients maintain their BG levels during ICU (level A) at less than 180 mg/dL and that insulin infusions are the most efficient way to maintain glucose control (level A).

They further suggest that postprandial BG levels in the step-down unit should also be preserved at less than 180 mg/dl (level B) with oral agents if previously prescribed or subcutaneous basal and bolus insulin therapies, such as glargine and lispro. Both of our insulin infusion trial patients in the latest study maintained a BG level of 150 mg/dL - 180 mg/dL for the first 48 hours.

The NICE-SUGAR research was recently completed and the results suggest that in this massive, international, randomized trial, intensive glucose regulation improved mortality among adults at the ICU. The investigators found that there was an appropriate level of less than 180 mg/dL for achieving a BG goal. (NICE-SUGAR Research Investigators, 2009).

5.9 Limitations

The data collected from one center for cardiac surgery, also there is no identified protocol for glucose level, the study not evaluated the effectiveness of glycemic control over 3 month time before surgery.

Recommendation

In hospitals, which is in line with current STS recommendations, we recommend that all patients who have undergone CABG should have a more liberal BG target level of 150 to 180 mg/dl.

Nursing implications

Good perioperative glycemic control, which blood glucose between 150-180 mg/dl without increased risk of hypoglycemia and sternal infection can be achieved. Healthcare professionals can integrate these results into their own methods based on our own and others' experiences.

Conclusion

Maintaining blood glucose levels (150-180) with continuous insulin infusion at all stages of the perioperative period will minimize the incidence of surgical site infection, episodes of hypoglycemia, stroke, pneumonia and length of stay in ICU and hospital in patients undergoing CABG surgery.

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Annex I: Data collection sheets

A target blood glucose of 150-180 mg/dL

Glucose level mg/dl	**Regimen**
Less than 70	**Notify physician, Discontinue drip and follow hypoglycemia guidelines**
70-100	**0 unit/hour**
101-120	**2.5 units/hour**
121-150	**4.5 units/hour**
151-200	**6 units/hour**
201-250	**8 units/hour**
251-299	**9 units/hour**
More than 300	**Notify physician**

Patients are managed intra-operatively with insulin drip (Michaelian, 2011).

Adjust the infusion rate according to the above regimen

Blood glucose monitored every 30 minutes

In the case of cardioplegia, cooling and rewgrouping of the patient take blood glucose every 15 min.

Blood glucose level mg/dl	**Regimen**
Less than 80	**Notify physician , discontinue drip and follow hypoglycemia guideline**
150-200	**6 units/hr**
201-250	**8 units/hr**
251-299	**9 units/hour**

Postoperative in CCU (Michaelian, 2011)

Blood glucose monitored every one hour

Adjust the infusion rate according to the ordered regimen.

Monitoring blood glucose levels hourly during insulin therapy until blood glucose levels are in the target range for 3 hours, then monitoring levels every 2 hours. Hourly blood glucose testing is resumed if levels are out of the target range or if the patient's clinical condition changes significantly.

When the patients are ready to be released from the ICU, patients should switch to a subcutaneous insulin dosing schedule. Daily insulin requirements can be estimated by extrapolating the amount of insulin required in the previous 24 hours and considering the patient's current nutritional intake (Furnary et al., 200; Schmeltz et al., 2006).

Demographic Data

Variables	Values	
Age (year)		
Gender (male/female)		
Weight (kg)		
Height (cm)		
BMI		
Ejection Fraction %		
History of MI	□ Yes	□ No
History of arrhythmia	□ Yes	□ No
History of atrial fibrillation	□ Yes	□ No
History of smoking	□ Yes	□ No
Pre-operative blood glucose		
Duration of surgery		
Duration of anesthesia		
Preoperative blood glucose		
hemoglobin A1c		

Intra-operative blood glucose measurements

Blood glucose monitored every 30 minutes

In the case of cardioplegia, cooling and rewgrouping of the patient take blood glucose every 15 min.

Adjust the infusion rate according to the ordered regimen

Time	**Blood glucose value**

Postoperative blood glucose measurement

Blood glucose monitored every one hour

Adjust the infusion rate according to the ordered regimen.

Monitoring blood glucose levels hourly during insulin therapy until blood glucose levels are in the target range for 3 hours, then monitoring levels every 2 hours. Hourly blood glucose testing is resumed if levels are out of the target range or if the patient's clinical condition changessignificantly.

Time	Blood glucose values

Outcomes measures

Variable	Results
Sternal wound infection	□ Yes □ No
Urinary tract infection	□ Yes □ No
Superficial sternal infection	□ Yes □ No
Deep sternal infection	□ Yes □ No
urinary tract infections	□ Yes □ No
Pneumonia	□ Yes □ No
Readmission	□ Yes □ No
In-hospital mortality	□ Yes □ No
Cardiac complication	□ Yes □ No
Stroke	□ Yes □ No
Acute renal failure	□ Yes □ No
Hypoglycemia	□ Yes □ No
ICU-LOS (days)-	
Postoperative hospital LOS (days)	

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جامعة
النجــاح الوطنية
كلية الدراسات العليا

التاريخ : 2019/11/10م

حضرة الدكتور يوسف التكروري مدير المستشفى الاهلي المحترم

الخليل

تحية طيبة و بعد ...

الموضوع : تسهيل مهمة الطالب/بلال بلاصي، رقم تسجيل (11659432).
تخصص ماجستير تمريض العناية المكثفة

الطالبة / بلال بلاصي رقم تسجيل 11659432، تخصص ماجستير تمريض العناية المكثفة، في كلية الدراسات العليا، وهي بصدد اعداد الاطروحة الخاصة بها والتي عنوانها:

(The effectiveness of tight glycemic control on reducing surgical site infection in diabetic patients undergoing coronary artery bypass grafting)

يرجى من حضرتكم تسهيل مهمته في قسم العناية المكثفة في مستشفى الخليل لتعبئة استمارات للمرضى الموجودين في قسم العناية المكثفة، وكذلك الاطلاع على بعض ملفات سابقة لمرضى أجريت لهم العملية قبل الدراسة، وذلك لاستكمال مشروع البحث.

شاكرين لكم حسن تعاونكم.

مع وافر الاحترام ،،،

أ.د. ناجي قطناني

عميد كلية الدراسات العليا

د. يوسف عبد الحميد التكروري
المدير العام
المستشفى الأهلي - الخليل

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جامعة
النجـــاح الوطنية
كلية الدراسات العليا
مكتب العميد

التاريخ: 2020/8/23

حضرة الدكتورة عائدة القيسي المحترمة
منسقة برامج ماجستير التمريض

تحية طيبة وبعد،

الموضوع : الموافقة على عنوان الاطروحة وتحديد المشرف

قرر مجلس كلية الدراسات العليا في جلسته رقم (395) المنعقدة بتاريخ 2020/8/19، الموافقة على مشروع الأطروحة المقدم من الطالب/ة بلال رباح حسين بلاصي، تسجيل 11659432، تخصص ماجستير تمريض العناية المكثفة، عنوان الأطروحة:

(تنظيم نسبة السكر في الدم اثناء عملية ترقيع شرايين القلب وبعدها وتأثير ذلك على التهاب مكان العملية)
(The Effectiveness of Tight Glycemic Control on Reducing Surgical Site Infection in Diabetic Patients Undergoing Coronary artery Bypass Grafting)

بإشراف: د. عائدة القيسي

يرجى اعلام المشرف والطالب بضرورة تسجيل الاطروحة خلال اسبوعين من تاريخ اصدار الكتاب. وفي حال عدم تسجيل الطالب/ة للاطروحة في الفترة المحددة له/ا ستقوم كلية الدراسات العليا بإلغاء اعتماد العنوان والمشرف

وتفضلوا بقبول وافر الاحترام ،،،

د. عوني ابو حجلة
عميد كلية الدراسات العليا

نسخة : د. رئيس قسم الدراسات العليا للعلوم الطبية والصحية المحترم
: أ.ع. القبول والتسجيل المحترم
: مشرف الطالب
: ملف الطالب

ملاحظة: على الطالب/ة مراجعة الدائرة المالية (محاسبة الطلبة) قبل دفع رسوم تسجيل الاطروحة للضرورة

An-Najah
National University
Health Faculty of medicine&
Sciences
IRB

جامعة النجاح
الوطنية
كلية الطب وعلوم الصحة
لجنة اخلاقيات البحث العلمي

IRB Approval Letter

Study Title:

"The effectiveness of tight glycemic control *on reducing surgical site* infecton in diabetic patients undergoing *Coronary artery bypass grafting* "

Submitted by:
Bilal Balassi

Supervisors:
Dr. AidahAlkaissi

Date Reviewed:
29th Oct. 2019

Date Approved:
31st Oct. 2019

Your Study titled "The effectiveness of tight glycemic control *on reducing surgical site* infecton in diabetic patients undergoing *Coronary artery bypass grafting* " *with archived number (39) Oct. 2019 was reviewed by An-Najah National University IRB committee and was approved on 31th Oct. 2019*

Hasan Fitian, MD

IRB

IRB Committee Chairman
An-Najah National University

جامعة النجاح الوطنية

كلية الدراسات العليا

تنظيم نسبه السكر في الدم أثناء عمليه ترقيع شرايين القلب وبعدها وتأثير ذلك على التهاب مكان العملية

إعداد

بلال بلاصي

إشراف

د. عايدة أبو السعود القيسي

قدمت هذه الاطروحة استكمالاً لمتطلبات الحصول على درجة الماجستير في برنامج تمريض العناية المكثفة، بكلية الدراسات العليا، في جامعة النجاح الوطنية، نابلس–فلسطين.

2021

تنظيم نسبه السكر في الدم أثناء عمليه ترقيع شرايين القلب وبعدها وتأثير ذلك على التهاب مكان العملية

إعداد

بلال بلاصي

إشراف

د. عايدة أبو السعود القيسي

الملخص

مقدمة

يرتبط مرض السكري بزيادة معدلات الاعتلال والوفيات الجراحية. قد تكون المخاطر العالية نسبيًا مرتبطة بمستوى ارتفاع السكر في الدم قبل العمليات الجراحية. يعد التحكم في نسبة السكر في الدم في مرضى القلب بعد الجراحة أمرًا ضروريًا لتحسين نتائج عدوى الجروح والوفيات الإجمالية. في السنوات الأخيرة، وجدت التجارب السريرية التي قيمت التحكم في نسبة السكر في الدم في المرضى المصابين بأمراض خطيرة من خلال الإدارة المكثفة لنسبة السكر في الدم انخفاضًا كبيرًا في معدلات الإصابة بالأمراض والوفيات. نشرت بعض المنظمات توصيات لإدارة السكر في الدم في المرضى ذوي الحالات الحرجة تعكس هذه المعلومات. ومع ذلك، فقد وجدت التجارب السريرية الجديدة التي تقيم المناطق المستهدفة للسكر في الدم في المرضى المصابين بأمراض خطيرة نتائج متضاربة، مما أدى إلى إعادة تقييم الأهداف والإرشادات الحالية، مما يتيح مناطق مستهدفة أقل صرامة لسكر الدم. مع التناقض في التجارب السريرية التي تقيم نطاق سكر الدم للمرضى ذوي الحالات الحرجة، وخاصة مرضى جراحة القلب بعد الجراحة، لا يزال سكر الدم المثالي غير محدد بشكل واضح. من شأن المقارنات الإضافية لنطاقات السكر المحددة أن تسمح بتعريف أوضح لأهداف سكر الدم الموصي بها لمرضى القلب بعد الجراحة.

الهدف

الهدف من هذه الدراسة هو تقييم فعالية تدخلات التحكم في نسبة السكر في الدم المحكم أثناء العملية وبعد العملية الجراحية مع ضخ الأنسولين المستمر للحفاظ على مستويات السكر في الدم

من 150–180 مجم / ديسيلتر للحد من مضاعفات جراحة القلب المفتوح، أي. إعادة الادخال، وفيات المستشفى، ومدة الإقامة، والإقامة في المستشفى، وحدوث نقص سكر الدم (مستويات السكر في الدم ≤70 مجم / ديسيلتر) في مرضى السكري البالغين الذين يخضعون لعمليات القلب المفتوح. المادة والطريقة: دراسة شبه تجريبية أجريت على مرضى السكري الذين يخضعون لعملية تحويل مسار الشريان التاجي الاختيارية. أجريت تجربة سريرية أحادية المركز بين مرضى السكري، ذكور 86 وإناث 14، تتراوح أعمارهم بين 18–70 عامًا مع ASA II– III الذين يخضعون لعملية تحويل مسار الشريان التاجي من المستشفى الأهلي، الخليل– فلسطين. ينقسم المرضى إلى مجموعة تجريبية مع ضبط محكم معدل (سكر الدم الذي تم الحفاظ عليه بين 150–180 مجم/ ديسيلتر) ومجموعة التحكم التي تلقت الأنسولين حسب البروتوكول للحفاظ على نسبة السكر في الدم تمت متابعة المرضى لمدة تصل إلى 48 ساعة بعد الجراحة. تم جمع حالات العدوى في الموقع الجراحي، وإعادة الادخال، والوفيات في المستشفى، ومدة الإقامة في وحدة العناية المركزة، ومدة الإقامة في المستشفى، وحدوث نقص سكر الدم (مستويات السكر في الدم ≤70 مجم/ ديسيلتر)، ومضاعفات أخرى في مرضى السكري البالغين الذين يخضعون لعمليات القلب المفتوح.

نتائج الدراسة

لا توجد فروق ذات دلالة إحصائية بين مجموعة التحكم والمجموعة التجريبية في الجنس والعمر والوزن والارتفاع ومؤشر كتلة الجسم قيم $P> 0.05$ أظهرت النتائج عدم وجود فرق معنوي في متوسط سكر الدم قبل الجراحة في مجموعة التحكم 38.76 ± 185.22) M ± SD) مقارنة بالمجموعة التجريبية 173.72 ± 18.74 (ع = 0.063). على عكس هذه النتيجة، أظهرت النتائج أن متوسط الهيموجلوبين A1c في مجموعة التحكم (المتوسط = 9.12) أقل بكثير من ذلك في المجموعة التجريبية (المتوسط = 9.71) (ع = 0.003).

أظهرت النتائج أن متوسط جلوكوز الدم أثناء العملية في مجموعة التحكم ± 223.03) M ± SD (47.32 أعلى بكثير من ذلك في المجموعة التجريبية) (2.64 ± 170.91) M ± SD ع = 0.000.

كما أظهرت النتائج أن متوسط نسبة السكر في الدم بعد العملية الجراحية في مجموعة التحكم (المتوسط = 283.08) أعلى بكثير من ذلك في المجموعة التجريبية (المتوسط = 168.88) (ع = 0.000).

أظهرت النتائج أن عدد المرضى الذين أصيبوا بعدوى قصية عميقة في مجموعة التحكم8) 4 = ٪ (أعلى بكثير من ذلك في المجموعة التجريبية 0 (0٪) (ع = 0.041). كما أظهرت النتائج أن عدد المرضى الذين أصيبوا بالالتهاب الرئوي في مجموعة التحكم) 8٪ 4 =٪ ((أعلى بكثير من ذلك في المجموعة التجريبية) N ٪0) 0 = (٪ (((ع = 0.041). كما أظهرت النتائج أن عدد المرضى الذين أصيبوا بسكتة دماغية في المجموعة التاريخية8.2) 4 =٪ ((أعلى بكثير من ذلك في المجموعة التجريب0) 0 = ٪) (ع = 0.039

أظهرت النتائج أن متوسط المكوث في العناية المكثفة (أيام) في مجموعة التحكم (المتوسط = 4.14) أعلى بكثير من ذلك في المجموعة التجريبية (المتوسط = 2.18) (ع = 0.000). كما أظهرت النتائج أن متوسط الخروج من المستشفى بعد العملية الجراحية (أيام) في مجموعة التحكم (المتوسط = 5.72) أعلى بكثير من متوسط المجموعة التجريبية (المتوسط = 4.98) (ع = 0.000).

استنتاج

إن الحفاظ على مستويات السكر في الدم (150–180) مع ضخ الأنسولين المستمر في جميع مراحل الفترة المحيطة بالجراحة سيقلل من حدوث عدوى موقع الجراحة ونوبات نقص السكر في الدم والسكتة الدماغية والالتهاب الرئوي ومدة الإقامة في وحدة العناية المركزة والمستشفى في المرضى الذين يخضعون لعمليات القلب المفتوح.

الكلمات المفتاحية

تحويل مسار الشريان التاجي، جراحة القلب، عدوى الموقع الجراحي، التحكم في نسبة السكر في الدم، الأنسولين، نقص السكر في الدم، ارتفاع السكر في الدم، عمليات القلب المفتوح.