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Decreasing the Risk of Post-operative Morbidity Through the Use of Glucose-Insulin-Potassium Infusion During Cardiac Surgery: An Educational Module for Anesthesia Practice

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Decreasing the Risk of Post-operative Morbidity Through the Use of Glucose-Insulin-Potassium Infusion During Cardiac Surgery: An Educational Module for Anesthesia Practice

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Abstract

Background: Coronary artery bypass surgery (CABG) is a conventional treatment method for people with coronary artery disease and acute coronary syndrome (ACS). Unfortunately, compared to patients with stable angina pectoris, these individuals have higher myocardial infarction (MI) risks, hospital readmissions, and high rates of cardiac mortalities after surgery. The glucose-insulin–potassium (GIK) method has been utilized in diverse therapeutic contexts for nearly five decades to reduce ischemic myocardial injury due to its cardio protective metabolic and non-metabolic measures. There are notable benefits of using the GIK method to reduce myocardial injury and improve hemodynamic performance in ACS patients undergoing cardiac surgery. GIK infusion prior to myocardial ischemia enhances myocardial ischemia resistance. GIK plays a major role in protecting cardiac tissues from hypoxia by ensuring the maintenance of normal glucose and metabolism of fatty acid and cell function. An educational model describing the benefits of GIK during CABG is proposed for anesthesia providers as a means of improving the quality of practice and leading to better patient outcomes.

Keywords: Glucose insulin potassium, GIK, Cardiac surgery, CABG, myocardial protection, morbidity

Introduction

Background

Cardiovascular disease (CVD) is the leading cause of death worldwide, accounting for approximately 30% of all mortality in 2019.[1,2] In the United States alone, over 126 million adults were diagnosed with CVD between the years of 2015 and 2018, estimating a total cost of $363.4 million annually.[2] While lifestyle modifications including diet, weight loss, smoking cessation, exercise, and pharmacology help attenuate CVD, many of these same patients require cardiac surgery. Coronary artery-bypass surgery (CABG) is a well-established treatment option for coronary artery disease or acute coronary syndrome (ACS) patients. Unfortunately, low cardiac output syndrome is common in this group, affecting 5-15% of patients after cardiac surgery.[3] Systemic hypoperfusion, poor ventricular function, the requirement for inotropic assistance, and mechanical support are all symptoms of low cardiac output syndrome. Although aerobic metabolism provides energy to cardiac myocytes, anaerobic metabolism is the primary fuel source during heart surgery. Additionally, there is an increase in free fatty acids during anaerobic metabolism, which may exacerbate the ischemic injury.[1]

Unfortunately, compared to patients with stable angina pectoris, these individuals have higher myocardial infarction (MI) risks, hospital readmissions, and high rates of cardiac mortalities after cardiac surgery. Off-pump CABG (OPCAB) has recently resurfaced as a treatment option for high-risk patients, as it has been linked to a better outcome than on-pump CABG.[2] As a result, a successful myocardial infarction protection approach, particularly for a high-risk population, such as acute coronary syndrome patients who require immediate surgical revascularization, is vital.

With such staggering data, it is no surprise that cardiac surgery has employed multiple techniques and interventions for myocardial protection since such surgery was pioneered in the 1950s.[3] The glucose-insulin–potassium (GIK) strategy has been implemented in a range of therapeutic circumstances to decrease ischemic myocardial injury for decades because of its heart-protective metabolic and non-metabolic characteristics. Adopting the GIK strategy for reducing myocardial-injury and improving hemodynamic-performance in ACS patients having cardiac surgery was reported to be beneficial by Bothe et al in 2004.[4] The major metabolic process is the efficient provision of glycolytic adenosine triphosphate, which is crucial for preserving membrane integrity during ischemia.[4] As a result, GIK infusion prior to myocardial ischemia enhances myocardial ischemia resistance.

The reduction of circulating free fatty acids is another putative critical metabolic process. This reduction encourages glucose as a predominant source of myocardial fuel, which consumes smaller amounts of oxygen and causes less damage to the tissue.[4] The heart's oxidative reserve is drained due to ischemia, which also steadily depletes phosphates rich in energy. [4] GIK plays a major role in protecting cardiac tissues from hypoxia by ensuring the maintenance of normal glucose and metabolism of fatty acid and cell function.

Problem Statement

Cardiac surgery, like many other medical specialties, is pushing the frontiers of medicine. The population of patients undergoing cardiac surgery is growing older, and surgical procedures have become more sophisticated, which has resulted in increased comorbidity. Further, the myocardium in these patients is frequently underperforming. Cardiac remodeling caused by myocardial ischemic procedures frequently leads to low ejection fractions, which intensifies the risks of low cardiac output in the early recovery period after cardiac operation.[3] Numerous

strategies have been used to improve myocardial protection, with varying degrees of success.[3] Cardioplegia's structure, temperature, and delivery method are among the major debated topics by cardiac surgeons. Continuing research initiatives include pharmacological therapies and the biocompatible materials used in the control of inflammatory responses elicited by surgery and cardiopulmonary bypass procedures.[4] The hunt for simple, inexpensive strategies to increase myocardial protection and outcome continues as interventions aimed at reducing ischemia/reperfusion injury struggle to translate promising outcomes from experiments into daily clinical practice.

Significance

With an incidence of 5-15%, low cardiac output syndrome is a serious complication for patients undergoing cardiac surgery.[3] Low cardiac output syndrome encompasses a myriad of complications including systemic hypoperfusion, worsening ventricular function, the need for inotropic support, and mechanical support.[3] During open heart surgery, the myocardium is susceptible to ischemia and ischemia reperfusion injury.[3] The myocardial myocyte normally obtains its energy from aerobic metabolism; however, during cardiac surgery, the major fuel source is obtained anaerobically.[4] During anaerobic metabolism, there is an increase in free fatty acids which can worsen the ischemic injury.[3] This recognition is crucial since it can result in an earlier identification and treatment measures.

Myocardial ischemic injuries that occur after heart surgery can increase the risks of both morbidity and mortality.[3] Even in patients who have no electrocardiogram abnormalities, ischemic injuries might induce some myocardial cell death. A clinically detectable type of such damage is perioperative myocardial infarction, which has a negative impact on the patient’s outcome.[4] Myocardial ischemia-reperfusion injury causes myocardial shock, reperfusion

arrhythmias, endothelial dysfunction, and irreversible cell death, which leads to myocardial infarction, left ventricular failure, and death.[4] Angina pectoris is the most evident medical sign of myocardial ischemia, regardless of its cause. Angina can occur without myocardial ischemia, and angina can occur without apparent indications of myocardial ischemia. Anginal pain is usually retrosternal and has a severe, pressing, or scorching sensation. The throat, neck, ulnar side of the left and right arm, inter-scapular region, epigastrium, jaw, and teeth may all be affected.[4] With or without angina, dyspnea, palpitations, syncope, or cardiac arrest are all possible outcomes of myocardial ischemia. This demonstrates that the consequences related to cardiac surgery are severe hence the need for an intervention measure to reduce ischemia and myocardial injury during cardiac surgery.

Knowledge Gaps

Increasing experimental evidence has shown that GIK provides significant cardiac protection after surgery in ischemic hearts.[1,3-15] Clinical trials, on the other hand, have not consistently proven that this medication is helpful, mainly due to differences in GIK formulations and delivery timing in these investigations.[4,6-7,10] In prior GIK formulations, the insulin-to-glucose ratio was typically between 1:6 and 1:4, resulting in a considerable blood glucose increase in GIK patients.[4] Although the appropriate degree of glycemic management in patients undergoing cardiac surgery and other critically ill patients is still debated, perioperative hyperglycemia is commonly linked to a poor result in patients undergoing cardiopulmonary bypass (CPB). There is also a lack of knowledge on the effects of myocardial protective effects of GIK in patients with ACS undergoing OPCAB.[4]

Myocardial preservation has been a critical component of the effective outcome of cardiac surgical procedures since the first developed in the 20th century. Even though many

alternative strategies for myocardial preservation and modulation have been documented over the last 50 years, the use of glucose, insulin, and potassium (GIK) continues to play a significant role in cardiac surgery. After heart surgery, GIK may help patients restore contractile function more quickly.[5]

In addition, GIK may help in reducing the risk of atrial fibrillation after cardiac surgery. GIK has therefore been proposed as a way of reducing mortality rates and improving post-cardiac surgery recovery.[5] Cardiac surgery with hypothermic cardioplegic arrest induces some myocardial cell death, even for patients with smooth recovery and no electrocardiogram abnormalities. A clinically detectable form of such injury, perioperative myocardial infarction, has a negative impact on the patient's outcome. Research[5] also shows that an infusion of GIK can help the heart heal faster and reduce ischemic injury after bypass surgery.

Indeed, numerous benefits of GIK have been noted. First, during ischemia, the substrate supply to the cells has a glycogen-sparing impact.[5] Additionally, there is a boost in the synthesis of adenosine triphosphate (ATP). During hypoxia, there is a reduction of phosphates rich in energy, such as adenosine triphosphate, while glycolysis is critical for maintaining cardiac viability.[5] Adenosine triphosphate by oxidative phosphorylation is favorably utilized to sustain myocyte contractile action by delivering energy to the actin-myosin-ATPase.[5] The myocardium's primary energy source is oxidative oxidation of free fatty acids under normal conditions. The free fatty acids oxidative metabolism returns after reperfusion, but it appears to be impaired following ischemia.[5] GIK also helps maintain the function of the sarcoplasmic reticulum and calcium homeostasis. Putative compartmentation of glycolytic and oxidative ATPase is another reason for GIK's protective effect. As a result, glycolysis-derived ATP is critical for sarcoplasmic reticulum (SR) function recovery after hypoxia.[5] In addition to a scavenging of free

radicals, there is also a decrease in the concentration of free fatty acids.[5] This is a side effect of insulin. Under hypoxic conditions, free fatty acids can disrupt cell membranes, resulting in calcium excess, arrhythmias, and cell death. Finally, there is increased myocardial perfusion due to decreased coronary artery resistance.[5]

A patient's cardiogenic shock and cardiac reserve may also benefit from GIK. Cardiopulmonary bypass (CPB) is a procedure used to keep blood flowing during heart surgery. However, CPB is linked to several organ issues, including hyperglycemia caused by neuroendocrine stress. On research study[5] found that stress-induced hyperglycemia led to a worsening of outcomes for patients undergoing heart surgery. Patients benefit from intraoperative and postoperative glycemic management and perioperative therapy using GIK with a 1:3 insulin-glucose ratio had favorable benefits after cardiac surgery in a pilot study of 40 valve replacement cases.[5]

Literature Review

Background

Numerous studies demonstrate glucose-insulin-potassium (GIK) as a potent cardioprotective intervention, but clinical trials have yielded mixed results, likely because of varying formulas and timing of GIK treatment and different clinical settings.[6] Most patients who have undergone coronary artery bypass surgery (CABG) have diastolic dysfunction due to the procedure. Left ventricle (LV) diastolic chamber stiffness increased after CABG, according to pressure-area correlations derived from synchronous hemodynamic and transesophageal echocardiographic (TEE) monitoring.[7] Reduced LV compliance may be due to severe global ischemia and post-ischemic revascularization during CABG, production of oxygen-free radicals throughout cardiopulmonary bypass (CPB), method of cardioplegia delivery, changes in LV

geometry with the open or closed pericardium, drugs used, or physical factors due to sternal closure that cause the decrease in LV compliance.[7]

When the myocardium becomes ischemic followed by reperfusion, glucose is a better energy source than free fatty acids. At that time, a GIK solution was discovered by Sodi-Pallares et al[8] to minimize electrocardiographic alterations in patients with acute myocardial infarction. According to Licker et al[6], studies in individuals with acute myocardial infarction and after cardiac surgery have revealed that GIK positively impacts the ischemic myocardium's myocardial performance.[6] It has been demonstrated that GIK intravenous therapy may enhance cardiac indices, reduce the requirement for inotropic support during surgery, minimize weight gain, reduce time on a ventilator, reduce stay in the intensive care unit (ICU), and decrease atrial fibrillation incidence in CABG patients.[6]

Rationale

A GIK infusion, together with strict glycemic control, improves ventricular function after bypass, alleviates myocardial injuries, and reduces the incidence of cardiac and respiratory complications after CABG and aortic valve replacement (AVR) surgery.[9] Given its safety and efficacy profile, this GIK-induced cardioprotective mechanism can serve as a valuable adjunct to the current myocardial protection strategy, especially in medium and high-risk patients undergoing open heart surgery.

Methodology

Eligibility Criteria

The studies included in this literature review were chosen to identify the current advances on GIK and its effects on reducing postoperative morbidity after surgery. The studies were selected using both inclusion and exclusion criteria. In addition, the studies were published in the

last 20 years and had full text available. The database sources utilized for this research were accessed via Florida International University (FIU) library services. A thorough search was conducted using the Cumulative Index to Nursing and Allied Health Literature (CINAHL), PubMed, and ProQuest.

Results of Individual Studies Supporting GIK

Licker et al[6] conducted a secondary assessment of randomized controlled trials with a quantitative experimental approach, seeking to evaluate the impact of GIK on the performance of the left ventricle when patients with aortic stenosis were undergoing valve replacement. Their focus was to assess the risk of patients suffering from ischemia-reperfusion injuries during cardiac surgeries. The methodology applied a randomized trial for moderate to high-risk patients who were to receive GIK or saline over 60 minutes after being anesthetically induced. The primary observation was an early change in 2- and 3-dimensional left ventricular ejection fraction, the transmittal flow propagation velocity, and the peak global longitudinal statin. The results led to the understanding that administering GIK before an aortic cross-clamping led to better systolic and diastolic ventricular function preservation in patients who need aortic valve replacement in left ventricular hypertrophy.[6]

Licker et al[6] demonstrate that the aortic valve replacement has been a standard treatment procedure for some time for patients who have severe aortic valve stenosis.[6] In these procedures, however, there must be an infusion of GIK to maximize the myocardial injuries that a patient undergoing open-heart surgery might sustain. The authors[6] have identified that the addition of GIK therapy to the common cardio-protection mechanisms when dealing with medium to high-risk patients with severe aortic valve stenosis was largely responsible for the improved preservation of left ventricle systolic and diastolic function. This enhanced post-bypass left

ventricular function. The GIK-treated patients were positioned for a better long-term clinical outcome due to a favorable remodeling of the LV. It subsequently reduces the inotropic drug requirement support after the AVR and during the recovery period.[6]

Licker et al[10] took a quantitative approach to examine whether the use of a GIK infusion improved the performance of the ventricles after a patient had undergone CABG surgery. The study was driven by the fact that most poor recovery and outcomes following heart surgery result from heart failure. The research methodology employed a randomized control trial to assess the effects that GIK had on the left ventricle functioning in moderate to high-risk patients who have been subjected to on-pump isolates coronary artery bypass surgery. The primary observation was an early change in the 2- and 3-dimensional left ventricular ejection fraction to transmittal flow propagation velocity and the peak global longitudinal statin. The GIK administration was observed to cause favorable interaction effects. The research found that the use of GIK led to better preservation of the diastolic and systemic ventricular functioning following wearing from CPB.[10]

Licker et al[10] further assert that the developed world is experiencing huge morbidity and mortality due to cardiovascular diseases. As a result of this condition, most patients require myocardial revascularization procedures, which have changed significantly in the last few decades. Endothelial dysfunction and left ventricular hypertrophy are major issues that warrant care in surgical procedures to successfully prevent myocardial ischemia-reperfusion damages that raise the risk of a surgery going wrong. Licker et al[10] found that several mechanisms such as the sodium/calcium exchange activity, were responsible for the GIK induced enhancement of ventricular contractility in low oxygen demand levels. However, the sensitization of and increased beta-1 adrenergic receptors heightens myoplasmic calcium availability, which

increases monophosphate substrate. Finally, GIK suppresses surgically induced inflammation responses that may result from reduced C-reactive protein levels, a tumor necrosis factor-alpha responsible for cardiac contractile dysfunction.[10]

Bruemmer-Smith et al[11] conducted a quantitative experimental study that measured CABG using hypothermic cardiac arrest and CPB and associated with myocardial injuries. The study's main objective was to determine if a GIK infusion in elective CABG surgery would lead to a decline in cell death in the myocardium. The methodology took the approach of measuring the troponin sensitivity and indicator capability of myositis injury. A total of 42 patients were enrolled and separated into 2 groups. In the first group, 500ml of a 50% dextrose solution was infused, while the other group received a 5% dextrose solution. The arterial blood samples were taken before anesthesia and after removing the aortic clamp. The results showed no rise in the cTnl concentration, which peaked about 6 hours after the CPB.[11] It was noted that the cTnl level did not differ between the 2 groups.[11] It was conclusive that GIK did not decrease the irreversible myocardial damage that surgery for routine coronary artery bypass caused.[11]

According to Breummer-Smith et al,[11] during ischemia, a patient's heart experiences a limited reserve of phosphates that are rich in energy that becomes subsequently steadily depleted. Patients experiencing hypoxia, when subjected to GIK, can maintain aerobic metabolism protection of the myocardial tissue by regulating carbohydrate and fatty acid metabolism.[11] During myocardial ischemia and reperfusion, the effects of GIK are complex. Currently, cardiac surgery conducted with hypothermic cardioplegia arrest may cause myocardial cell death; hence GIK has no protective functionality during cardiac surgery using bypass. However, GIK offers other benefits that include supplying the substrate during ischemia into the cells. It also increases

the synthesis of ATP and maintains the functionality of the sarcoplasmic reticulum and the homeostasis of calcium.[11]

Zhao and coauthors[3] conducted experimental quantitative research demonstrating GIK intervention as a potent cardio-protective following clinical trials. This research study[3] evaluates the impact of a modified GIK regimen in patients undergoing cardiopulmonary bypass surgery. However, the clinical trials gave mixed results due to different clinical settings and variable timing and formulas of GIK treatment. The methodology involved randomized, double-blinded, and prospective trials involving 939 patients identified for cardiac surgery with placebo treatment and CABG.[3] Both groups, those given the placebo and those given the GIK infusion, were found to experience arrhythmias, congestive heart failure, cardiac arrest with resuscitation, acute myocardial infarction, and low cardiac output.[3] The GIK therapy significantly reduced adverse cardiac incidences and improved cardiac-function recovery with no increased perioperative blood-glucose than the control group.[3]

The method analysis in this research[3] involves a comparable population between both groups. The 2 groups did not differ significantly regarding previous medical history such as myocardial infarction, smoking, hypertension, and preoperative medications like statins, digitalis glycosides, and B-Blockers.[3] This study implements the European system of cardiac stratification risks, and the scores for the groups were relatively similar, 4.19 and 4.24, in the GIK group and control group respectively. The levels of lactate and blood glucose over time were analyzed using mixed models as studying subjects and surgeons as random effects.[3] GIK therapy treatment increased glucose uptake with less lactase excretion and GIK-regimen performed preoperatively decreases the in-hospital worst cardiac incidences, especially in patients undergoing cardiopulmonary bypass. It is evident that during reperfusion and ischemia,

the heart breaks down endogenous glucose or increases circulating glucose to maintain glycolytic flux, which is essential for preserving cellular viability. These benefits improve the perfusion of systemic tissue while improving the metabolism of the myocardial through insulin activation signaled by GIK.[3]

Ahmad et al[12] explore the relationship between myocardial protection with GIK during adult cardiac surgery. Critical analysis of this article classifies it as non-experimental, quantitative research because there is no control group. The main objective of this research was to evaluate the effectiveness of a GIK solution in patients who are non-diabetic but underwent coronary artery bypass grafting, as recent reports on meta-analysis had encouraged more randomized trials to determine the GIK solution's effectiveness in cardiac surgery patients.[12] Indeed, there is a need to select the relationship between cardiac patients and the efficacy of GIK solutions.

The study results indicate that the CK-MB peak levels were high in the early postoperative period in the non-GIK group 48.5, while the GIK group was 33.40.[12] Between the 2 groups, there was no statistically significant difference in inotropic support requirements. In the non-GIK group, the mean duration of inotropic support was 8.6 hours, while in the GIK group was 5.50 hours.[12] The results also indicated GIK intrusion's detrimental effect on non-cardiac complications like neurologic, pulmonary, and renal complications.[12] The researchers randomized a total of 160 patients into 2 equal groups. The participants were classified into GIK and non-GIK groups. Among the GIK group, 70 meq/L of potassium and 70 IU/L regular insulin-containing 5% dextrose was administered. The infusion began at the rate of 30ml per hour before the start of cardiopulmonary bypass and after induction of anesthesia. These authors

concluded that GIK infusion is essential in myocardial protection, providing positive postoperative outcomes without increasing non-cardiac complications.[12]

Ellenberger et al[7] conducted a randomized controlled trial among adult patients undergoing surgery to replace the aortic valve or bypass to determine the effect of GIK in enhancing myocardial protection among patients with moderate to high risks while undergoing on-pump heart surgery. Post-cardiotomy ventricular dysfunction was the primary endpoint, while intraoperative change was the secondary endpoint of this research. The results indicate that 222 were analyzed: 110 were GIK groups, and 112 were placebo. The pretreatment of GIK was associated with PCVD reduction in occurrence with a confidence interval of 0.25.[7] The left systolic ventricular function among the GIK treated patients was preserved better after weaning from plasma troponin and bypass levels. The respiratory and cardiovascular complications were reduced, thus leading shorter stays in the intensive care unit.[7]

The researchers[7] concluded that GIK pretreatment was associated with attenuation of PCVD, and clinical outcomes improved among the moderate and high-risk patients in the process of on-pump cardiac surgery. The limitation of this study is that the GIK solution was provided only at a fixed dose and was only limited to the pre-bypass period, thus becoming challenging to determine the continuation of GIK-infusion. Also, the primary study outcome and the diagnosis of PCVD were based on subjective operator-independent criteria.[7]

The primary objective of Tsang et al[13] was to determine whether the perioperative GIK infusion's clinical benefit is mediated through a reduction in diastolic dysfunction severity, which occurs after CABG.[13] A total of 31 patients undergoing CABG surgery were randomized at the time of enrollment into 2 categories: 14 receiving GIK and 17 non-GIK. The measure of LVEDA was made at PCWP constant level. The patients enrolled included those undergoing non-

emergent CABG for the first time. for gaining either GIK infusion or non-GIK. The administration of infusion was done through a central venous catheter which was initiated 30 minutes before the sternotomy and stopped during CPB.[13]

The GIK group resulted in a reduction in LVEDA from 17.0 ml to 15.3ml, while in the case of the non-GIK group, LVEDA reduced from 17.5 ml to 14.3ml.[13] In addition, the deceleration time of the doppler transmittal wave E was shortened because of the rapid equilibrium of LV and LA pressure. The researchers concluded that diastolic dysfunction happens almost universally after CABG and that chest closure worsens it by persisting for up to 3 hours without any effects from GIK. Therefore, the clinical benefits have no relation with the diastolic dysfunction's amelioration despite theoretical reasons for GIK limiting perfusion injury and ischemia.[13]

El-Hakeem et al[14] conducted a randomized clinical trial to analyze the efficiency of the GIK solution in myocardial protection assessed by postoperative cardiac troponin I and CK-MB levels. The year-long research entailed the identification of patients over 30 years-old who had coronary artery bypass grafting on cardiopulmonary bypass. The study[14] excluded: patients with poorly controlled diabetes mellitus, patients who underwent off-pump surgery, and patients with preoperative renal dysfunction. The study also excluded patients with severe liver disease, previous stroke, emergency CABG surgery, concomitant valvular heart disease, and poor cardiac functions.[14]

The patients were placed in 2 groups. The patients in 1 group were administered 100 ml of GIK solutions per hour, from the anesthesia to the end of the operation. The other group only received 0.9% normal saline with a similar infusion rate and volume as the GIK group. El-Hakeem et al[14] found lower values of all CK-MB in the GIK group than the non-GIK group.

Additionally, the GIK group had lower troponin values than the non-GIK group after 12 hours. However, troponin values were similar at 24 hours' samples.

El-Hakeem et al[14] concluded that GIK infusion and cardioprotective techniques in patients with CABG surgery on CPB reduce myocardial cell injury. However, the GIK solution was administered at a fixed dose, limiting the study's duration and observation. Another limitation of the research was that the decisions to extubate and discharge patients from the ICU followed established protocol that could impact the results. Lastly, the study was conducted in patients with good cardiac functions.[14]

Finally, Slob et al[15] conducted a retrospective audit to determine the extent to which GIK application at a London teaching hospital had on improving cardiac functioning during surgery among critically ill patients. These authors[15] further note that increasing doses of insulin as a part of the regimen were deemed to have substantial benefits, such that experiments eventually employed up to 1.0 units insulin/kg/hour with safe outcomes. Patients undergoing GIK at this hospital were treated with catecholamines and had their glucose and potassium levels measured prior to commencement of the procedure. After a bolus of glucose and insulin, patients were administered GIK infusion up to 1.0 units/kg/hour,[15] levels similar to those used by Zhao et al.[3]

Overall, high-dose GIK infusions were demonstrated to augment cardiac performance in patients, especially critically ill patients, along with improved blood lactate levels. Close monitoring of blood glucose and potassium levels is required, as a minority of patients did experience severe hypoglycemia, hyperglycemia, hypokalemia, or hyperkalemia.[15] However, because of proper monitoring protocols, such instances were quickly identified and treated.

Education of Anesthesia Providers

Given that the educational component of this project will take place in a virtual environment, it is worth investigating the success of such learning opportunities. Shah et al[16] explore the increasing prevalence of virtual-based education, specifically with anesthesia providers. These authors[16] particularly note the incentives towards sub-specialization among anesthesia providers, which often detracts from a provider's ability to provide more holistic care, including the effectiveness of GIK during cardiovascular surgery. Professional education through simulations and virtual learning environments are recommended as the ideal setting.[16]

According to Boggs and Luedi, the implementation of new technologies, new medicines, and a rapidly changing diversity of clinical settings requires that anesthesiologists receive specific training, including cognitive knowledge.[17] Henderson et al[18] argue that nurse anesthesia education specifically lacks certain educational experiences that work to increase clinical reasoning skills and expose them towards levels of self-directed learning. Deutsch and Straker, in exploring key concepts of patient safety for anesthesiologists, note the contemporary use of simulations and virtual education, especially in situations that could result in potential patient complications.[19]

Given the immediate nature by which education moved to a virtual environment because of the COVID-19 pandemic, Sneyd et al[20] specifically examined e-learning among anesthesia students. These authors note how socially distanced education modules allow for flexible access on demand on the part of the student, suggesting that online teaching may become the new normal across provider education in the field.[20] However, the researchers note the limitations that accompany online education with what still remains a craft specialty, in that anesthesiologists must learn through hands-on experience.[20] Given the specific nature of educating providers on a

specific regimen to be implemented during high-risk cardiac surgery, it can be argued that some of the limitations noted by these authors should be overcome in this project.

Discussion

The current literature has pointed significantly to the functionality and effectiveness of GIK in aiding cardiovascular surgery. GIK plays a significant role in protecting the left ventricle against ischemia-reperfusion that may arise from anomalies in the healing process.[3-15] GIK ensures a hormonal balance that allows it to attain full healing and move the patient through the healing process without incident. The primary outcome variables were the left ventricular ejection LVEF were measured through 2 and 3-dimensional echocardiographers, transmittal flow propagation velocity (Vp), and the peak global longitudinal strain (PGLS). The secondary measures provided, such as the TEE data used in some studies, proved that GIK has a protective functionality that increases patient healing after surgery and ensures that the left ventricle was protected during the surgical procedure.

Conclusion

Although the first application of a GIK infusion in cardiac surgery was over 40 years ago, its application today has yielded mixed results. There is substantial evidence that prove that a GIK infusion serves as a myocardial protectant. Details such as when to start the GIK infusion, how long to administer the infusion, and how its formulated are questions that remain unanswered and require further research. GIK enhances myocardial perfusion and ensures the activation of intracellular signaling pathways that block apoptosis and promote cell survival. This plays a significant role in decreasing myocardial injury during ischemia and reperfusion throughout cardiac surgery, hence reducing morbidity and mortality.

Purpose/PICO Clinical Question/Objectives

To translate the literature and to address the issue of a lack of anesthesia provider knowledge of the benefits of GIK in practice, the purpose, PICO (population, intervention, comparison, outcome) clinical question, and objectives for the project must be delineated. The purpose of this quality improvement project is to increase anesthesia provider use of GIK through provider training. The PICO clinical question formulated to guide this project is as follows:

- In anesthesia providers working in an acute care facility (**P**) who are provided with an educational module about adopting the Glucose Insulin Potassium infusion (GIK) strategy for reducing myocardial-injury and improving hemodynamic-performance (**I**), does the knowledge of GIK increase (**O**) as compared with their knowledge level before the educational module (**C**)?

Breaking this question down by respective P, I, C, and O elements, the following is observed:

- Population (P): anesthesia providers
- Intervention (I): Glucose Insulin Potassium infusion (GIK) strategy education
- Comparison (C): Knowledge before the educational intervention.
- Outcomes (O): Knowledge increase following the educational module.

Objectives

With the proliferation of research proving the effectiveness of GIK as a myocardial protectant during cardiac surgery, the primary goal of this project is to create an educational module for providers of cardiac surgery patients. The use of GIK as a myocardial protectant can be traced back nearly five decades; however, its use in the current clinical setting remains nonexistent. This module will serve to bring awareness of the positive impacts the GIK infusion

can bring to cardiac surgery by presenting the research findings of the literature review that was conducted.

Strengths

The facility that this project will be implemented in is one of the largest trauma facilities in south Florida, with a dedicated heart program. One of the main strengths of this facility, is its dedicated cardiac team that is comprised of cardiac nurses, cardiac surgical techs, cardiac surgeons, and cardiac anesthesia providers. In other facilities, the teams cross train staff and do not have a specific team dedicated to every specialty. Moreover, this facility's heart program does cardiac surgery, along with heart transplantation, and insertion ventricular assistive devices in both the pediatric and adult population. This hospital is the only facility in Florida with an accredited Adult Congenital Heart program; there are 17 hospitals throughout the United States with such distinct accreditation. The essential strength expected in developing a GIK educational module is unique to postoperative care among adult patients undergoing heart reconstruction and is in accordance with the organization's values, vision, and mission. The organization's interest is to emphasize passionate team care whose advancement method is to care for children and adults while supporting families. This is done by guiding empathy, transformation, advocacy, empowerment, responsibility, and collaboration.

Weakness

While this facility's strengths are solid in their dedicated program and team members, there are several weaknesses that may limit its successful implementation. One main weakness is the heart protocol that has been in place for over 15 years. When the protocols were first tried and implemented, they included the latest evidence-based practice guidelines of its time. Since then, there has been a proliferation of research on cardiac surgery complications and different

modalities to employ for myocardial protection. Despite the latest guidelines fluctuating with current recommendations changing, this facility has not made any changes to its current protocol. Change is always difficult, especially in an organization that runs a successful heart program and is known nationwide. It is evident that many clinicians within the organization have inadequate knowledge regarding the different modalities that can be used for myocardial protection.

Opportunities

One crucial opportunity at this facility is increasing the baseline knowledge of myocardial protection during cardiac surgery. Due to the current guidelines in place, many providers fail to think outside of what is presented in the guidelines. In addition, the providers often fail to do research and learn more about the latest evidenced-based information available, as they are aware that implementing changes can be a difficult endeavor. Another opportunity with this project would be decreasing the morbidity of patients post cardiac surgery. While the heart program is successful and one of the few nationwide, it can also be the first to employ the GIK adjunct during cardiac surgery and serve by leading other facilities in the country to implement the changes. It is evident that providers must have a basic understanding of the GIK adjunct, and their responsibilities in the execution and importance of the program.

Threats

Various factors may interfere with or harm the process and the ability of the program for achieving its objectives. These program's risks may include negative feelings of the providers towards GIK protocols because of potential deviation from the existing care standards. Research done by Tsang et al,[13] indicates that most providers fear that such care standards may damage their autonomy in provision of patient care, which is individualized, especially when the patients are not meeting goals of treatment. Moreover, another threat of this project could include the

lack of participation from the providers due to their resistance of change. The resources and logistics necessary for such an endeavor also serve as potential threats for the success of this program. These authors[13] also emphasizes the importance of leadership amongst clinicians, which will promote an effective work environment whereby evidence-based practice procedures are supported and encouraged to improve organizational compliance.

Since the success of GIK implementation depends significantly on the compliance of the participants, the providers must show engagement in the possibility of an updated protocol which may be unique from existing operations. Lastly, there must be clarity on what the program entails for maximum buy-in from the clinicians and surgeons involvement. For instance, if the goal of GIK therapy is to reduce the length of hospitalization, health care providers must be satisfied with their ability of caring for their patient after discharge.

Definition of Terms

The specific terms required to understand this DNP project are defined here in order to provide additional clarity regarding the full extent of the proposed practice change. Particularly, the following terms were noted to need clarification:

- Myocardial protection – In its simplest definition, the term myocardial protection encompasses the multiple techniques employed during cardiac surgery to protect the heart from ischemia and reperfusion injury that occurs with aortic cross clamping and cardioplegia.
- CABG – Coronary artery bypass grafting surgery is a procedure that is used to treat patients with coronary artery disease and ACS. In this procedure, vessels harvested from a different part of the body are used to divert blood flow past these obstructions, and revascularize the tissue.

- Morbidity – Morbidity is the suffering of a disease or illness, both mental and physical, that can have a negative impact on quality of life.

Theoretical Framework

The theoretical model chosen for this project was that of Kurt Lewin's change theory. According to Hussain et al,[21] Lewin's Change Theory is a 3-step model consisting of unfreezing, changing, and refreezing stages. In order to initiate change, a foundation must be prepared for the required change, which begins in the unfreezing stage.[22] During the change stage, the conditions are implemented that move towards the desired outcome.[22] Once change has been reached, the refreezing stage requires that new procedures and activities are made a permanent part of organizational operations.[22]

Theory Overview

Under Lewin's theory, the unfreezing first step requires the creation of an awareness of how the current state of affairs is ineffective, or even hindering the organization in some manner.[23] It is during this stage that an organizational assessment should be undertaken, so that all relevant stakeholders can see first-hand the necessity of change within the organization.[23] Informing stakeholders during this first step is vital in order to prevent, or at least reduce, resistance to change on the part of individuals. Clear and constant communication is particularly vital at this juncture, because effective communication imparts to all stakeholders the reasons why change is necessary, the impending changes they will experience, and the benefits, both personal and organizational, they will gain as a result of the change.[23]

During the change stage, the organization moves from an old state of operations into a new state.[23] It is in this stage that the determined change is implemented for the good of the organization. Once again, communication is vitally important, so that stakeholders have an easier

time completing the change. Stakeholders also need support and education so that they can become more familiar and comfortable with the changes.[23] The more information and education that stakeholders receive during this step, the more likely it is that change will become an ingrained part of the new way of doing things. Finally, in the refreezing stage, the change is reinforced and solidified within the organization.[23] It is especially important that, once change has been made, people do not revert back to the old ways of operation.[23]

Clinical Fit

Through the application of Lewin's Change Theory to this proposed DNP project, it should be possible to ensure optimal outcomes through changes in knowledge levels among anesthesia providers regarding the efficacy of GIK with high-risk cardiac patients. Lewin's theory is appropriate when attempting to determine how effective and organization will be in modifying its procedures.[21] Lewin's model allows for a thorough understanding of the current state and a road map whereby to achieve a future, desired state, through the unfreezing of old ways, implementation of a change, and refreezing of behaviors so that the change is reinforced.[22]

Methodology

The Program Structure

The process of GIK development requires multidisciplinary and collaborative team efforts. It is essential to involve all stakeholders during the formulation stages of this project. This is because there will be increased dissemination of information since every stakeholder will have new information about the pros and cons of the method. A comprehensive assessment of the environment will be performed to determine the locality of opportunities and the significance, value, and importance of the project to every stakeholder within the organization.

Since this study aims to examine provider knowledge of clinical practices of patients who have undergone cardiac surgery, the initial step will be to identify an expert team from the stakeholders. Specifically, this team of expert stakeholders will be responsible for guiding the development of the educational intervention and GIK protocols. Under this, participants will be provided first with questionnaires for measuring their knowledge of GIK protocols, well-established treatment options, coronary artery bypass protocols and off-pump CABG procedures. Participants will answer the questions provided in the questionnaires separately to avoid bias in the collected information. Participants will be given an educational program that addresses patient care with heart problems who have undergone coronary artery bypass through GIK protocols. This study will be provided to all participants using an online platform. After interventions, participants will be requested to survey the variations in the skills and knowledge of the educational program.

Settings and Participants

The setting of the entire educational module will be virtual, consisting of an online educational model to be accessed by the participants. For the purpose of this query, the participation of cardiac surgery providers will be solicited through an initial recruitment letter sent via email to a list of anesthesia providers at Memorial Regional Hospital in Broward County. The educational module will include a pre-test, PowerPoint presentation, and a post-test. The educational module and both tests will be delivered virtually through an online platform to the anonymous providers who volunteer to participate in this educational endeavor.

Description of approach and project procedures

The first step of implementing this project will consist of a recruitment letter sent via email which will include the purpose of the project, the specific expectations, details, dates, and

deadlines. The email will also include a link to a survey for those who wish to participate to collect demographic data. After completing the survey, the participants will have access to the educational module, beginning with the pre-test. The pre-test will consist of questions to establish the provider's current knowledge of myocardial protection, cardiac surgery complications, and GIK infusion. The PowerPoint presentation will be available after completion of the pre-test for the participant to review. The presentation will include a synopsis of the literature, tables summarizing the findings, the role of glucose in aerobic metabolism of the cardiac myocyte, and the statistics of cardiac surgical complications. The final part of the educational module will be a post-test with similar questions to the pre-test, to determine if there is an increase in knowledge.

Protection of human subjects

The participation of cardiac surgery providers will be solicited for this project; however, their participation will be completely voluntary and anonymous. The survey collecting demographic data and the answers to both tests will be kept anonymous using random identification coding. As this scholarly project is an educational module, there is no perceived risk for participants. There will be no testing or experimentation conducted with live patients.

Data collection and management

The data collection and data management will be handled by the co-investigator of this project, a Doctor of Nursing Practice candidate. The author will compose the initial email including the recruitment letter and survey, create a PowerPoint, and develop pre- and post-tests for the educational module. The surveys and test will be delivered using Qualtrics, a web-based platform. At the completion of the implementation phase, the pre- and post-tests will be evaluated using statistical analysis to assess the effectiveness of the educational program.

Discussion of the results and implications to advanced nursing practice

The results of this project should increase the providers knowledge on the use of GIK as an adjunct to the current myocardial protection modalities. It should also bring awareness to the complications that can occur post cardiac surgery, including risk factors and signs and symptoms of such complications. Furthermore, at completion of the educational model, the participants will have a chance to provide feedback on the strengths and weaknesses of the entire module, and on whether they would consider using GIK as an adjunct for myocardial protection in the future.

Further, it has been noted that advanced practices nurses serve as leaders and must work to improve the overall healthcare system.[24] Given that there are real benefits to using GIK during cardiac surgery, it would seem logical to suggest that this project will allow for the more widespread use of this technique in practice, which will better the profession holistically.[25]

Conclusion

For the success of the implementation of this GIK educational module for cardiac surgery, the providers will have to keep an open mind, especially because the use of it remains nonexistent in the United States. First, there will be an email for recruitment of participants entailing the programs specifics, overall goals, and deadlines for completion of the module. The PowerPoint will include flowcharts, and visualizations on the latest research findings of GIK as a myocardial protectant and the common complications post cardiac surgery. The collected data will undergo analysis and comparison with the expectations and goals devised at the planning-phase through a review of charts that assess the differences in the pre and post test scores. The participants will be interviewed at the evaluation phase for obtaining input on the program's overall effectiveness. In addition, the author will be expected to give a summary of the program evaluation's primary findings. The expected report must be clear and detail the program, data

collection and analysis methods, purpose statement, and intervention used. The report should also entail significant findings, recommendations on program improvement, design flaws, unexpected or unanticipated outcomes and conclusions.

Results from Implementation

Participant Demographics

There was a total of 4 participants, 3 (75%) females and 1 (25%) male. Age groups included 2 (50%) participants between 30 – 39 years old, and 2 (50%) participants between 50 – 59 years old. The ethnicity of the participants were 2 (50%) White/Caucasian, 1 (25%) Hispanic, and 1 (25%) African American. Fifty percent (50%) 2 participants had a Master's degree, and 2 (50%) had a Doctorate degree. There were varying years of experience amongst the providers, with 2 (50%) having between 2-5 years, 1 (25%) 5-10 years, and 1 (25%) 10 years plus.

Participant demographics are displayed in table form below.

Total Participants	**4**
Gender	
Male	1 (25%)
Female	3 (75%)
Age	
20 – 29	0 (0%)
30 – 39	2 (50%)
40 – 49	0 (0%)
50 – 59	2 (50%)
60+	0 (0%)
Ethnicity	
African American	1 (25%)
Asian	0 (0%)
White/Caucasian	2 (50%)

Hispanic	1 (25%)

Level of Education	
ASN	0 (100%)
BSN	0 (100%)
MSN	2 (50%)
Doctorate	2 (50%)

Years of Experience	
1 – 2	0 (0%)
2 – 5	2 (50%)
5 – 10	1 (25%)
10+	1 (25%)

Pre-Test: Assessment of Baseline Knowledge

The Pre-Test was delivered to the participants prior to viewing the PowerPoint Presentation to determine their baseline knowledge. The questions on the Pre-Test and Post-Test were identical. Both tests were comprised of multiple-choice and true or false questions. The questions were as follows:

1. Approximately what percentage of mortality can be attributed to cardiovascular disease?
2. Approximately how many cardiac procedures are performed annually?
3. Cardioprotective strategies include:
4. What percentage of cardiac surgical patients experience postoperative complications?
5. Myocardial ischemia and ischemia-reperfusion injuries can cause:
6. True or False. Glucose-Insulin-Potassium (GIK) infusions were first used five decades ago in patients with acute coronary syndrome (ACS) undergoing revascularization.
7. Experimental studies have proven GIK infusions have _____ effects.
8. GIK therapy _____ myocardial lactate released at early reperfusion, improving cardiac cell metabolism.

9. GIK therapy decreases morbidity and increases cardiac hemodynamic performance by?
10. How likely are you to use GIK therapy as an adjunct for myocardial protection during cardiac surgery?
11. How likely are you to recommend GIK intravenous therapy?

For the tenth question, 1 (25%) participant answered “somewhat likely”, 2 (50%) participants answered “neither likely or unlikely”, and 1 (25%) participant answered “somewhat unlikely”. Lastly, for the eleventh question, 3 (75%) participants answered “neither likely or unlikely” and 1 (25%) participant answered “somewhat unlikely”.

Participants Pre-Test Results are displayed in table form below.

Participant #	Correct Answers	Score
#1	3/9	33.3%
#2	3/9	33.3%
#3	1/9	11.1%
#4	4/9	44.4%

Post-Test: Assessment of Learning

The Post-Test was administered at the conclusion of the educational Power Point presentation. The purpose of the Post-Test was to determine if any learning occurred, comparing the Pre-Test scores to the Post-Test. Additionally, the Post-Test was meant to ascertain of the anesthesia providers would consider incorporating GIK into their own practice.

Participants Post-Test Results are displayed in table form below.

Participant #	Correct Answers	Score
#1	7/9	77.8%
#2	8/9	88.9%
#3	5/9	55.6%
#4	8/9	88.9%

For the tenth question of the Post-Test, 2 (50%) participant answered, “somewhat likely”, 2 (50%) participants answered, “neither likely or unlikely”. Lastly, for the eleventh question, 2 (50%) participants answered, “somewhat likely”, 1 (25%) participant answered “somewhat unlikely”, and 1 (25%) participant “neither likely or unlikely.”

Implementation Discussion

The virtual education module produced significant positive results, with all participants attaining a higher score on their Post-Test after the Power Point presentation. There was an overall average increase of 47.3% when comparing both sets of scores. In addition, the number of participants “somewhat likely” to incorporate GIK into their future practice increased from 25% to 50%. For the last question about recommending GIK, there was an increase of “somewhat likely” responses from 25% to 50%.

Table comparing Pre & Post-Tests

Participant #	Pre-Test Score	Post-Test Score	Difference
#1	33.3%	77.8%	+44.5%
#2	33.3%	88.9%	+55.6%
#3	11.1%	55.6%	+44.5%
#4	44.4%	88.9%	+44.5%

Limitations

One of the most obvious limitations of this project was its small sample size. The anesthesia group this project was presented to has over 50 providers, including both MDs and CRNAs. In a practice with so many providers, and a dedicated cardiac anesthesia team, it seems as though a true opportunity was missed. Another glaring limitation was the delivery of the project being fully web-based with an email invitation. An email invitation can easily be sorted

into a junk folder or missed all together. Also, given the delivery, there was little ways to ensure that the participants completed the entire module with little to no distractions.

Implications for Future Anesthetic Practice

This extensive literature review demonstrates the use of GIK during cardiac procedures reducing morbidity and mortality. Despite the proliferation of research, GIK is seldomly used as an adjunct in cardiac anesthesia protocols. There is a lack of information regarding its proper dosage and timing of administration.

This educational module demonstrated that anesthesia providers are open to different learning formats and platforms. In addition, it also revealed that some anesthesia providers are willing and open to adjusting their current practice to increase positive patient outcomes. It is notable that there should be future research into the use of GIK for cardiac procedures, focusing on decreasing overall morbidity and mortality.

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Office of Research Integrity
Research Compliance, MARC 414

MEMORANDUM

To: Dr. Arturo Gonzalez

CC: Daniella Narvaez

From: Elizabeth Juhasz, Ph.D., IRB Coordinator EJ

Date: April 19, 2022

Protocol Title: **"Decreasing the Risk of Post-operative Morbidity Through the Use of Glucose-Insulin-Potassium Infusion During Cardiac Surgery: An Educational Module for Anesthesia Practice"**

The Florida International University Office of Research Integrity has reviewed your research study for the use of human subjects and deemed it Exempt via the **Exempt Review** process.

IRB Protocol Exemption #: IRB-22-0164 **IRB Exemption Date:** 04/19/22
TOPAZ Reference #: 111584

As a requirement of IRB Exemption you are required to:

1) Submit an IRB Exempt Amendment Form for all proposed additions or changes in the procedures involving human subjects. All additions and changes must be reviewed and approved prior to implementation.
2) Promptly submit an IRB Exempt Event Report Form for every serious or unusual or unanticipated adverse event, problems with the rights or welfare of the human subjects, and/or deviations from the approved protocol.
3) Submit an IRB Exempt Project Completion Report Form when the study is finished or discontinued.

Special Conditions: N/A

For further information, you may visit the IRB website at http://research.fiu.edu/irb.

EJ

Pretest and Posttest Questionnaire:

Decreasing the Risk of Post-operative Morbidity Through the Use of Glucose-Insulin-Potassium Infusion During Cardiac Surgery: An Educational Module for Anesthesia Practice

INTRODUCTION

The primary aim of this QI project is to improve the knowledge of CRNAs pertaining to the role of Glucose-insulin-potassium (GIK) infusions decreasing morbidity during cardiac surgery. Please answer the question below to the best of your ability. The questions are either in multiple choice or true/false format and are meant to measure knowledge and perceptions on the use of a GIK infusion as an adjunct for myocardial protections.

PERSONAL INFORMATION

1. **Gender:** Male Female Other
2. **Age:** 20 – 29 30 – 39 40 – 49 50 – 59 60+
3. **Ethnicity:** Hispanic Caucasian African American Asian Other
4. **Level of Education:** Associates Bachelors Masters Other
5. **How many years have you been an anesthesia provide?**

   Over 10 5-10 years 2-5 years 1-2 years

QUESTIONNAIRE

12. **Approximately what percentage of mortality can be attributed to cardiovascular disease?**

a. 20%

b. 30%

c. 50%

d. 70%

13. Approximately how many cardiac procedures are performed annually?

a. 500,000

b. 1,000,000

c. 1,500,000

d. 3,000,000

14. Cardioprotective strategies include:

a. Hypothermic cardiac arrest with potassium enriched solutions

b. Pharmacological preconditioning

c. Pharmacological postconditioning

d. All the above

15. What percentage of cardiac surgical patients experience postoperative complications?

a. 10%

b. 15%

c. 20%

d. 25%

16. Myocardial ischemia and ischemia-reperfusion injuries can cause:

a. Shock

b. Arrythmias

c. Endothelial dysfunction

d. Irreversible cell death

e. All of the above

17. Glucose-Insulin-Potassium (GIK) infusions were first used five decades ago in patients with acute coronary syndrome (ACS) undergoing revascularization.

True or False

18. Experimental studies have proven GIK infusions have _____ effects.

a. apoptotic

b. inflammatory

c. antiapoptotic

d. oxidative

19. GIK therapy _____ myocardial lactate released at early reperfusion, improving cardiac cell metabolism.

a. increases

b. reduces

c. has no effect

20. GIK therapy decreases morbidity and increases cardiac hemodynamic performance by?

a. Lowering incidence of low cardiac output syndrome

b. Reducing the need for inotropic support

c. Reducing the need for mechanical support

d. All of the above

21. How likely are you to use GIK therapy as an adjunct for myocardial protection during cardiac surgery?
    a. Most likely
    b. Somewhat likely
    c. Somewhat unlikely
    d. Most unlikely
22. How likely are you to recommend GIK intravenous therapy?
    a. Most likely
    b. Somewhat likely
    c. Somewhat unlikely
    d. Most unlikely