Research Article
ISSN: 0974-6943

Available online through
http://jprsolutions.info

A study on the Outcomes of Modified Tight Glucose Control for the Management of Glycemic Control in Diabetic Patients Undergoing Cardiac Surgery

FatemehJavaherforooshZadeh[1,2*], Mohammad Ghazi Nour[3]

[1]Associate Professor of Anesthesia, Department of Cardiac Anesthesia,Ahvaz Anesthesiology and Pain Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.
[2]Atherosclerosis Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.
[3]Assistant Professor of Cardiac Surgery, Department of Cardiac Surgery, Shiraz University of Medical Sciences, Shiraz, Iran.

Received on:14-09-2016; Revised on: 25-10-2016; Accepted on: 04-11-2016

ABSTRACT

Background and Objective: Diabetes mellitus is associated with increased surgical morbidity and mortality.Its relatively high risk may be related to the level of perioperative hyperglycemia. Thisstudy was aimed to compare the outcomes of patients undergoing open cardiac surgery byglucose control in two ways: modified tight versus conventional method. **Methods:** This open-labeled, randomized control trial was conducted on 75diabetic patients (18-70 years old) with ASA II- III undergoing open cardiac surgery from Shahid Faghihi Hospital, Shiraz, Iran. The patients were randomly divided into modified tight control(Blood Sugar maintained between 100-120 mg/dl) and conventional method (Blood Sugar ≤ 200mg/dl). Primary end points included**:** hospitalmortality, sternal wound infection, duration of mechanical ventilation, cardiacarrhythmia, cerebrovascular attack and acute renal failure. The secondary end point waslength of ICU staying. Complications after 30 days of surgery were recorded. We used student's t test, chi-squareand repeated measurement tests. **Results:** Although the trend of change in blood glucose during surgery and in ICU was notsignificantly different between groups, blood sugar measurement showed a significantdifference at the different times (P<0.001). In terms of primary end pointsandsecondary end pointwere not significantly different between two groups. The occurrence of hypoglycemiawas low in both groups (one patient in each group) and were not significantly different between two groups.Hypokalemia was the most prominent sideeffect in the 34 patients of modified tight control group compared with eight patients in theconventional group (P<0.001). After 30 days sternal wound infection was seen in1 patient oftreatment group versus 7 in control group (P<0.05), which was significant. **Conclusion:** Modified tight control of blood glucose close tonormal values during cardiac surgery was associated with decreased occurrence of episodes of hypoglycemia andhyperglycemic complications.

KEYWORDS: Cardiac surgery, Diabetes; outcome, Glycemic control

1. INTRODUCTION

Diabetes mellitus is associated with increased surgical morbidity and mortality. Its relativelyhigh risk may be related to the level of perioperative hyperglycemia.About 30-40% of patients, who are undergoing coronary artery bypass graft, have diabetes mellitus ormetabolic syndrome and are at risk for hyperglycemia events[1].

Hyperglycemia leads to increased susceptibility to infection of the surgical wound,neurological injury, cardiac and renal damage, increased need for inotropic support anddeath[1-3]. Hyperglycemia is a major cause of formation of abnormal proteins through non-enzymatic glycosylation that leads to the worsening of neurological damage, global and focal cerebralischemia through anaerobic conversion of glucose to lactate, thus disrupting the cellular metabolism[4].

***Corresponding author.**
FatemehJavaherforooshZadeh
Associate professor of Anesthesia,
Department of cardiac anesthesia,
Ahvaz Anesthesiology and Pain Research Center,
Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

Furthermore, hyperglycemia increases the duration of hospital stay and costs. On theother hand, diabetic patients are more likely to revascularization, 24% more risk ofreadmission for heart-related problems and 44% more risk of readmission[5].

The incidence of coronary artery disease is greater indiabetic patients. Furthermore, impaired platelet function, fibrinolytic and impairedendothelial function are more common in these patients which leads to less graft patency ,increased preoperative mortality, and reduced short and long term post-operative survival[6].

Insulin acts as an anti-inflammatory agent by inhibiting proinflammatoryfactors and reduces inflammatory mediators[7].

Insulin regulates the L-arginine nitric oxide pathway, therefore, improvesvasodilatation and endothelial function, and increasing prostacyclinrelease, thus improves platelet function. On the other hand Insulin reduces apoptosis[8].

Several studies have shown that patients with acute coronary syndrome whopresent with hyperglycemia are at higher risk of in-hospital mortality[9,10]. Hyperglycemia is important in determining the outcomeof acute coronary syndrome in diabetic and non-diabetic patients[9,11]. Doenst, assessed the outcome of 6280 patients undergoingcardiac surgery and found that patients with blood glucose levels greater than 360 mg/dl hadhigher intra-operative morbidity and mortality[4]. In similar findings increased post-operative complications were observed due to increased blood glucose levels[12-15]. These studies strongly suggested that theincreased levels of blood glucose in the preoperative period contribute to higher postoperative morbidity and mortality in both diabetic and non-diabetic patients undergoingcardiac surgery. However, tight control of blood glucose can lead to hypoglycemia that canbe associated with neurological damage[16].

According to some other studies, this method cannot improve the outcome in patients with open heart surgery[17]. Modified tight control methodhas been proposed as a method to overcome this limitation. Therefore, the aim of this studywas to compare the postoperative outcome of patients undergoing open cardiac surgery intwo methods of blood glucose control: modified tight control versus conventional methods.

2. MATERIALS AND METHODS:

2.1. Study design and population:

This Open-labeled, randomized control trial was conductedon 75 diabetic patients, aged 18-70 years with ASA II- III undergoing open heart surgeryfrom Shahid Faghihi Hospital, Shiraz, Iran. Patients were divided into modified tight control (Blood Sugar maintained between 100-120 mg/dl) and conventional method (Blood Sugar ≤ 200 mg/dl).

2.2. Inclusion criteria:

Diabetic patients scheduled for non-emergency open cardiacsurgery and aged between 18 to 70 years, were included.

2.3. Exclusion criteria:

Patients with ketoacidosis or hyperosmolar coma, Redo surgery, patients with a history of cerebrovascular accident (CVA) or transient ischemic attacks(TIA), patients with EF<30% and patients with a history of liver or kidney disease ,wereexcluded from the study.

2.4. Study procedure:

After arrival to the operation room, standard monitoring included five-lead electrocardiography, pulse oximetry and arterial line for continuous monitoring of blood pressure and blood gases were used. After general anesthesia the patients were randomly allocated in two groups: modified tight glycemic control (MTGC), and conventional glucose control (CGC). After induction of general anesthesia, central venous catheter inserted, and baselineBS via an ACCU- check Active glucometer (Roche, Germany) was checked. In MTGC, if the blood sugar was above 120 mg/dl, an infusion of 50 units of regular insulin in 50 ml saline was started in order to maintain blood glucose between 100-120 mg/dl. Insulin dose was adjusted according to the Table 1. In CGC if blood glucose was equal or higher than 200mg/dl, patients were treated with insulin as follows: If blood sugar was 200-250mg/dl, 4units of regular insulin per hour will be administered until the blood glucose reached to 200mg/dl. If blood glucose was greater than 250mg/dl, 4 units of regular insulin per hourbegan and continued until blood glucose became less than 150mg/dl and maintainedd"200mg/dl[18].

Table 1. Insulin infusion protocol in modified tight glucose control group (19)

Serum Glucose Level, mg/Dl	Insulin Infusion Rate, U/h
<70	Off
70-109	1
110-119	2
120-149	3
150-179	4
180-209	5
210-239	6
240-269	8
270-299	10
300-329	12
330-359	14
>360	16

The dose and type of inotropes during weaning from CPB were recorded. In both groups,blood glucose was measured every 30 min until the end of the surgery. Insulin infusion in MTCG patients was discontinued after the surgery.

ICU glycemic controls in both groups were performed by conventional methods and BS level was maintained d≤200mg/dl as the protocol used in operation room in CGC group. In the ICUblood glucose was checked every two hours until 20 hours after the operation. During thisperiod, subcutaneous insulin or oral anti diabetic medication was not prescribed. The insulin administration protocol was discontinued 24 hours after surgery in both MTCG and CGC.

3. RESULTS:

Variables such as mortality, sternal wound infection, duration of mechanical ventilation, cardiac arrhythmias (Atrial fibrillation, Cardiac arrest, Heart block which require pace maker), cerebrovascular attack and acute renal failure (two-fold increase in baseline creatinine) were the primary outcomes and length of ICU stay was evaluated as a secondary outcome. Occurrence of hypoglycemia (blood glucose less than 60 mg/dl that treated with 50 cc of dextrose 50%) and hypokalemia (serum potassium less than 3meq/dl, so corrected with 20meq of potassium) were noted. Outcomes were determined by the ICU generalpractitioner that was unaware of the treatment. Furthermore, 30 days after discharge, patientswere visited by the surgeon and adverse events (the same as the primary outcomes) were recorded. This study was approved by the ethics committee of Shiraz University of medicalsciences and all patients signed the informed consent before study.

3.1. Statistics:

Statistical analyses were performed using SPSS V19. The results areexpressed as mean ± SD, and P<0.05 was considered as significant. Data about patients'baseline characteristics in MTGC and CGC, including age, weight, preoperative bloodglucose, preoperative ejection fraction, duration of surgery were analyzed using Student's t-test.Chi –square analyses were performed to detect the need to inotropic support, theincidence of hypoglycemia and hypokalemia, early postoperative events (sternal woundinfection, cardiac complication, atrial fibrillation, stroke, acute renal failure and death) andmorbidity after one month in MCGC and CGC. For comparing blood glucose in MCGC and CGC during surgery and in ICU repeated measurement test was used. Duration of themechanical ventilation and stay in ICU under the Mann Whitney U test were compared inMCGC and CGC.

This clinical study comprised 75 diabetic patients who underwent open cardiac surgery, andwere divided into two groups: Thirty eight patients in the MTGC group and 37 patients in the CGC.

In terms of baseline characteristics including age, weight, preoperative blood glucose,ejection fraction no statistically significant differences were found between the two groups(Table 2).

Table 2. Baseline data of patients in Modified Tight glucose control and Conventional glucose control

Details	Modified Tight glucose control (n=38)	Conventional glucose control (n=37)	P
Age, mean±SD(Year)	58.18±10.77	59.18± 8.91	0.66
Male gender (%)	17 (44)	13 (35)	
Weight, mean±SD (kg)	65.55 ± 12.65	66.13± 9.85	0.82
Preoperative BS , mean±SD (mg/dl)	190.68 ± 81.04	192.41 ± 80.47	0.92
EF, mean±SD (%)	51.05 ± 9.94	50.02± 8.30	0.63
History of hypertension, N (%)	26 (68)	24 (63)	0.74
History of MI, N (%)	18 (47)	12 (32)	0.18
History of arrhythmia, N (%)	2 (5)	2 (5)	1
History of AF, N (%)	0(0)	1 (2.7)	0.49
History of smoking, N (%)	6 (16)	8(21)	0.24
Duration of surgery, mean±SD(min)	221 ± 77	231 ± 82	0.65

SD:Standard deviation; BS:Blood sugar; EF: Ejection Fraction; MI: Myocardial Infarction; AF:Atrial Fibrillation

The mean duration of surgery was similar in both groups (221±77 in MTGC versus231±82 min in CGC). In MTGC group, 29 patients required inotropic support compared with 26 patients in CGC (P=0.55).

Although the trend of change in blood glucose during surgery was not significantly different between groups, BS measurement showed a significant difference at the different times(P<0.001, Figure1).

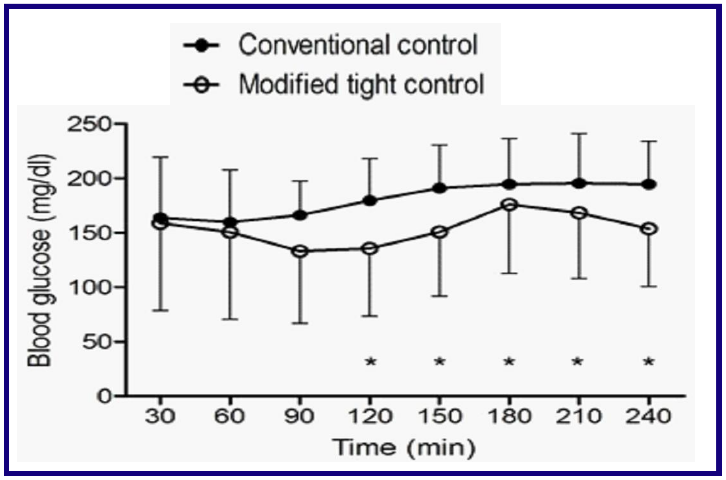

Figure 1.Comparison of trend of changes in the mean ± SD of the blood glucose levels in diabetic patients during cardiac surgery between Modified Tight glucose control and Conventional glucose control.* mean significant differences (P < 0.001).

Blood glucose level did not differ between the two groups in the ICU, but measuring the BSduring several hours showed a significant difference (P<0.001, Figure 2).

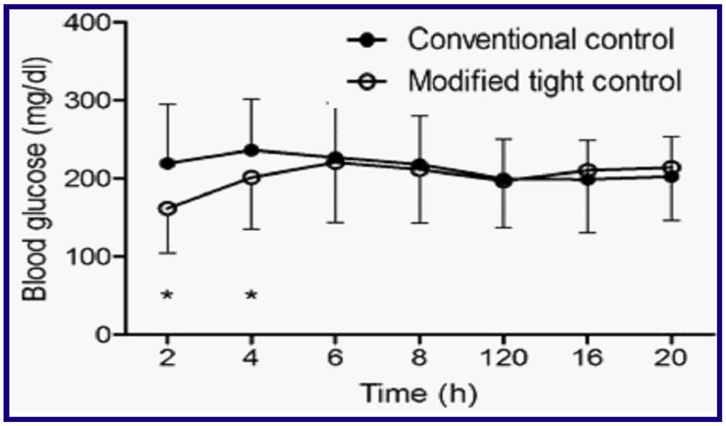

Figure 2.Comparison of trend of changes in the mean ± SD of the blood glucose levels in diabetic patients during ICU stay between Modified Tight glucose control and Conventional glucose control. *mean significant differences (P< 0.001).

During ICU, no significant changes in sternal wound infection, atrial fibrillation, cardiac complications, stroke, acute renal failure and death were observed. The occurrence of hypoglycemia was low in both groups (one patient in each group) and were not significantly different (Table3). However, hypokalemia was the most prominent side effect in the 34 patients of MTGC compared witheight patients in CGC (P<0.001) (Table3).

Table 3. Comparison of outcome in intensive care units in Modified Tight glucose control and Conventional glucose control

Complication in ICU	Modified Tight Glucose control (n=38)	Conventional Glucose control (n=37)	P
Sternal wound infection	0	2	0.24
AF	4	5	0.73
Cardiac complication	3	6	0.3
Stroke	1	1	1
Acute renal failure	1	1	1
Death	1	0	0.50
Hypokalemia	34	8	<0.001
Hypoglycemia	1	1	0.49

Except for significant sternal wound infection, one month after surgery (seven cases in aconventional versus one case in modified tight control) no differences between othercomplications in both groups were observed (P<0.05) (Table 4).

Table 4.Comparison of complications between Modified Tight glucose control and Conventional glucose control

Complication after one month	Modified Tight Glucose control (n=38)	Conventional Glucose control (n=37)	P
Sternal wound infection	1	7	<0.05
Foot infection	2	5	0.43
Cardiac complication	3	1	0.61
Stroke	0	1	1
Acute renal failure	1	3	0.6
Death	1	1	1

4. DISCUSSION:

The current clinical study was designed to compare the effect of glycemic control by twomethods: modified tight glycemic control and conventional on post-operative outcomes inthe diabetic patients after open cardiac surgery. We used insulin for modified tight glucosecontrol through a designed protocol to maintain BS in a range of 100-120 mg/dl in MTGC and ≤200mg/dl in CGC . In ICU both groups treated as a conventional method.

On the basis of previous studies[7,9,14,18], our hypothesis was based onimproving outcomes and reducing complications and thus, reducing the duration ofmechanical ventilation and length of ICU staying following TGC. It is reported that theadjustment of blood sugar in the range of 80-110 mg/dl through TGC and subsequent hypoglycemic episodes are responsible for the higher mortality rates[12,17,20,21].

Severe hypoglycemia is a medical emergency that may cause seizures and permanent braindamage. Likewise, hypoglycemia was defined as BS less than 40 mg/dl by Vandenberg. Also,physiological changes occur as follows: increasing the counter regulatory hormones if BS reaches to the 65mg/dl, adrenergic symptoms if BS was about 55mg/dl, and cognitive dysfunction in the BS around 45mg/dl[22]. The signs andsymptoms of hypoglycemia in patients undergoing surgery under general anesthesia andsedation in ICU are extremely difficult to determine. It seems that more studies are required for achieving the desirable level of blood glucoseduring surgery and in the ICU setting. Tight control of blood glucose can cause furtherlowering of blood glucose during surgery. Therefore, we decided to keep BS in the range of 100-120 mg/dl (modified TGC) to avoid hypoglycemia and its complications with the benefit of maintaining normal intra-operative blood glucose range.

In contrast to the previous studies that intra-operative tight glucose control (TGC) reducedthe complications, in our study early post-operative complications (sternal wound infection,atrial fibrillation, cardiac complications, stroke, acute renal failure and death) did not showany significant differences in the two groups (10 patients in MTGC 26% compared with 19 patients in CGC 51%). Hypokalemia in MTGC was significantly higher than in CGC (34 Versus 8 P<0.001).Insulin infusion results in hypokalemia and increase risk of dangerous arrhythmia asAF[23] . In our study, a significant increase in the incidence of hypokalemia wasfound in the treatment group (34 patients compared with eight patients) which caused alower number of AF rhythm (four cases compared with five cases) and lower incidences ofsinus tachycardia than in control groups. In the present study, despite of hypokalemia in MTGC group, AF rhythm and sinus tachycardia were lower in this group. This may be dueto better glucose control in this group and the desirability of controlling the blood glucoseduring the surgery. However, it deserves further study. Lazer divided 141 diabetic patientsundergoing CABG into two groups (administered infusion of the glucose-insulin-potassiumwith aims BS=125-200 mg/dl and standard with BS<250). Glucose Insulin Potassium (GIK) infusion started before induction of anesthesia and continued for 12 hours after surgery.

Patients, who received GIK, significantly had fewer AF rhythms (17% compared with 42%) and duration of hospital stay (6.5 vs. 9.2 days) was shorter. It should be considered that intheir study GIK was continued for 12 hours after surgery. So, in such cases administration ofthe potassium with insulin is recommended[24]. Vandenberg reported that 50 mg/dl lowering of blood sugar lead to 34% reduction of ICU mortality[22]. In our study, although the mean blood glucose in MTGCgroup at the end of surgery was approximately 38 mg/dl lower than the mean of CGC, postoperative complications in the ICU in both groups were not significantly different.

Our findings about primary outcomes were consistent with the results of Gunjan. Theystudied 400 diabetic and non-diabetic patients who were divided into two groups of the TGCgroup with the BS range of 80-100 mg/dl. Mean of BS at the end of surgery in the treatmentgroup was less than control group (114 mg/dl compared to 157 mg/dl). Forty four percent of patients inthe treatment group and 46% of patients in the control group encountered one of thesecomplications: Death (4 vs. 0), stroke (8 vs. 1) and a mean ICU stay of two days in bothgroups. In spite of the continuing insulin infusion in ICU, the post-operative mortality andmorbidity was not reduced[17].

Although in the present study the trend of change in blood glucose levels during surgerywas not significantly different in each group, they were significantly different from eachother at different times of measurement (from 90 to 240 min of starting the operation)therefore, differences in the blood glucose at the different hours of the surgery may notadequately reflect the favorable impact of modified tight control of blood sugar. Ghandisuggested that 20mg/dl increase in the average blood glucose leads to increase probability ofpost-operative complications for 34%[12]. In our study, the meanblood glucose levels were 160.64 ± 53mg/dl intra-operatively, and 208.20 ± 66.49 mg/dl post-operatively. While, the average blood sugar in Ghandi's study was 133 mg/dl. Complications such as death, stroke, and cardiac complications in TGC group were morethan the control group.

Salah divided 100 diabetic patients into two groups of TGC and common method that, tightcontrol of blood glucose was continued from the beginning of anesthesia to completerecovery of patients and extubation. Increasing in blood glucose level was continued untilthe end of the operation in the control group (with a mean of 227 mg/dl). Mean blood glucoselevels were similar in both groups before the start of CPB. However, significant differenceswere found between the two groups from the start of the CPB until extubation[25].

These findings were similar to our results at min of 90 (roughly the start of CPB) till the fourth postoperative hour (roughly the time of extubation).

Azarafarin studied the effect of tight control of blood glucose in non-diabetic patientsundergoing CABG. They concluded that for reducing complications of post cardiac surgery(from 32% to 16%), maintaining the blood glucose levels in the range of 110-126 mg/dl is needed[26].

We believe that the effect of mean BG levels according to the protocol was a definitedetermining factors in the dramatic decrease our infection rates. Deep sternal wound infectioncan cause increased mortality, length of hospital staying and retrieval of patient to theoperating room. Moreover, hyperglycemia increases the risk of deep sternal wound infectionby two folds. Insulin administration can enhance phagocytic functions of neutrophils andthus reduced infection in these patients. High blood glucose levels within the first 48 hours after surgery associated with sternal wound infection[27]. Long term follow up (after one month), showed one patient with sternal infection in MTGCand seven cases in CGC that was statistically significant result. It was similarly the study ofHruska, Smith et al. (2005)[28]. They indicated that continuous infusion of insulinadministrationto maintain BS=120-160 mg/dl, significantly reduced the rate of sternal wound infection inthe diabetic patients who underwent the CABG. Zerr, Furnary et al. (1997), divided 1585patients with diabetes into the control and protocol groups. The mean of BS in the protocolgroup was maintained within a mean of 176 mg/dl compared with the 195 mg/dl in the controlgroup. The incidence of wound infection in both sternal or foot ulcers were decreased from2.4% in the control group to the 1.5% in the treatment group. The Sternal wound infectionrate in the control group was only 2.8% compared with 0.74% in the treatment group[27]. Similarresults were found by Furnary, Zerrand Kramer[29,30]. While, theynoticed that sternal wound infection rate reduced in TGC method in diabetic patients in theircenter, who underwent open heart surgery (from 2.6% prior to the start of TGC method to1% after TGC method). Our study had some limitation, including small numbers of patients, this number does notrepresent the definite and accurate result;

therefore, further study is recommended with largerpopulations. In addition, one of the indices of cardiac event measurement is serum troponinlevel, it is recommended to evaluate this marker in future studies. We can conclude that theblood glucose can be maintained in the close range of normal by using a standard protocolwith insulin infusion. In the present study insulin infusion was discontinued at the end of thesurgery and to get better results, insulin infusion should be continued in the ICU at least untilthe need for inotropic support.

4. CONCLUSION:

We concluded that using a modified tight control of blood glucose level to a level that isclose to normal values during cardiac surgery may reduce episodes of hypoglycemia andthus reduces its side effects, as well as reduce hyperglycemic complications such as sternalwound infection.

Abbreviations:

ASA: American Society of Anesthesiologists,**MCGC:** modified tight glycemiccontrol,**CGC:** conventional glycemic control,**ICU:**Intencive Care UNIT,**TIA:**Transient Ischemic Attack,**EF:** Ejection Fraction, **CVA:**Cerebrovascular Accident,**CABG:**Coronary Artery Bypass Graft.

Competing interests:

The authors declare that they have no competing interests.

Authors contributions:

FJZ is responsible for the design of the research; MGN performed the experiments.

Acknowledgment:

This research was supported by Shiraz anesthesiology and critical care research center. Proposal No 91-01-60-5268 and IRCT2013041713052N1. The authors thank for Dr M.H PipelZadeh, Dr Z Forotan, Mr. Ghorbany, Dr M Heidari and all of nurse anesthesia of cardiac operating room and all of ICU nursing of Shahid Faghihi hospital.

REFERENCES

1. Gorter PM, Olijhoek JK, van der Graaf Y, Algra A, Rabelink TJ, Visseren FL, et al. Prevalence of the metabolic syndrome in patients with coronary heart disease, cerebrovascular disease, peripheral arterial disease or abdominal aortic aneurysm. Atherosclerosis. 2004;173(2):361-7.
2. Eagle KA, Guyton RA, Davidoff R, Edwards FH, Ewy GA, Gardner TJ, et al. ACC/AHA 2004 guideline update for coronary artery bypass graft surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1999 Guidelines for Coronary Artery Bypass Graft Surgery). Circulation. 2004;110(14):e340.
3. Kubal C, Srinivasan AK, Grayson AD, Fabri BM, Chalmers JA. Effect of risk-adjusted diabetes on mortality and morbidity after coronary artery bypass surgery. The Annals of thoracic surgery. 2005;79(5):1570-6.
4. Doenst T, Wijeysundera D, Karkouti K, Zechner C, Maganti M, Rao V, et al. Hyperglycemia during cardiopulmonary bypass is an independent risk factor for mortality in patients undergoing cardiac surgery. The Journal of thoracic and cardiovascular surgery. 2005;130(4):1144. e1-. e8.
5. Whang W, Bigger JT. Diabetes and outcomes of coronary artery bypass graft surgery in patients with severe left ventricular dysfunction: results from The CABG Patch Trial database. Journal of the American College of Cardiology. 2000;36(4):1166-72.
6. Carson JL, Scholz PM, Chen AY, Peterson ED, Gold J, Schneider SH. Diabetes mellitus increases short-term mortality and morbidity in patients undergoing coronary artery bypass graft surgery. Journal of the American College of Cardiology. 2002;40(3):418-23.
7. Langouche L, Vanhorebeek I, Vlasselaers D, Vander Perre S, Wouters PJ, Skogstrand K, et al. Intensive insulin therapy protects the endothelium of critically ill patients. The Journal of clinical investigation. 2005;115(8):2277-86.
8. Gao F, Gao E, Yue T-L, Ohlstein EH, Lopez BL, Christopher TA, et al. Nitric oxide mediates the antiapoptotic effect of insulin in myocardial ischemia-reperfusion the roles of PI3-kinase, Akt, and endothelial nitric oxide synthase phosphorylation. Circulation. 2002;105(12):1497-502.
9. Cheung NW, Wong VW, McLean M. The Hyperglycemia: Intensive Insulin Infusion In Infarction (HI-5) Study A randomized controlled trial of insulin infusion therapy for myocardial infarction. Diabetes Care. 2006;29(4):765-70.
10. Meier JJ, Deifuss S, Klamann A, Launhardt V, Schmiegel WH, Nauck MA. Plasma Glucose at Hospital Admission and Previous Metabolic Control Determine Myocardial Infarct Size and Survival in Patients With and Without Type 2 Diabetes The Langendreer Myocardial Infarction and Blood Glucose in Diabetic Patients Assessment (LAMBDA). Diabetes Care. 2005;28(10):2551-3.
11. Svensson A-M, McGuire DK, Abrahamsson P, Dellborg M. Association between hyper-and hypoglycaemia and 2 year all-cause mortality risk in diabetic patients with acute coronary events. European heart journal. 2005;26(13):1255-61.
12. Gandhi GY, Nuttall GA, Abel MD, Mullany CJ, Schaff HV, Williams BA, et al., editors. Intraoperative hyperglycemia and perioperative outcomes in cardiac surgery patients. Mayo Clinic Proceedings; 2005: Elsevier.

13. Székely A, Levin J, Miao Y, Tudor IC, Vuylsteke A, Ofner P, et al. Impact of hyperglycemia on perioperative mortality after coronary artery bypass graft surgery. The Journal of thoracic and cardiovascular surgery. 2011;142(2):430-7. e1.
14. Imran SA, Ransom TP, Buth KJ, Clayton D, Al-Shehri B, Ur E, et al. Impact of admission serum glucose level on in-hospital outcomes following coronary artery bypass grafting surgery. Canadian Journal of Cardiology. 2010;26(3):151-4.
15. Duncan AE, Abd-Elsayed A, Maheshwari A, Xu M, Soltesz E, Koch CG. Role of intraoperative and postoperative blood glucose concentrations in predicting outcomes after cardiac surgery. The Journal of the American Society of Anesthesiologists. 2010;112(4):860-71.
16. Albacker T, Carvalho G, Schricker T, Lachapelle K. High-dose insulin therapy attenuates systemic inflammatory response in coronary artery bypass grafting patients. The Annals of thoracic surgery. 2008;86(1):20-7.
17. Gandhi GY, Nuttall GA, Abel MD, Mullany CJ, Schaff HV, O'Brien PC, et al. Intensive intraoperative insulin therapy versus conventional glucose management during cardiac surgery: a randomized trial. Annals of internal medicine. 2007;146(4):233-43.
18. Smith CE, Styn NR, Kalhan S, Pinchak AC, Gill IS, Kramer RP, et al. Intraoperative glucose control in diabetic and nondiabetic patients during cardiac surgery. Journal of cardiothoracic and vascular anesthesia. 2005;19(2):201-8.
19. Hines RL, Marschall K. Stoelting's anesthesia and co-existing disease: Elsevier Health Sciences; 2012.
20. Arabi YM, Dabbagh OC, Tamim HM, Al-Shimemeri AA, Memish ZA, Haddad SH, et al. Intensive versus conventional insulin therapy: a randomized controlled trial in medical and surgical critically ill patients. Critical care medicine. 2008;36(12):3190-7.
21. Finney SJ, Zekveld C, Elia A, Evans TW. Glucose control and mortality in critically ill patients. Jama. 2003;290(15):2041-7.
22. Bruyninckx F, Schetz M, Vlasselaers D, Ferdinande P, Lauwers P, Bouillon R. Intensive insulin therapy in the critically ill patients. New England Journal of Medicine. 2001;345:13531367.
23. Kjeldsen K. Hypokalemia and sudden cardiac death. Experimental & Clinical Cardiology. 2010;15(4):e96.
24. Lazar HL, Chipkin SR, Fitzgerald CA, Bao Y, Cabral H, Apstein CS. Tight glycemic control in diabetic coronary artery bypass graft patients improves perioperative outcomes and decreases recurrent ischemic events. Circulation. 2004;109(12):1497-502.
25. Asida SM, Atalla MMM, Gad GS, Eisa KM, Mohamed HS. Effect of perioperative control of blood glucose level on patient's outcome after anesthesia for cardiac surgery. Egyptian Journal of Anaesthesia. 2013;29(1):71-6.
26. Azarfarin R, Sheikhzadeh D, Mirinazhad M, Bilehjani E, Alizadehasl A. Do nondiabetic patients undergoing coronary artery bypass grafting surgery require intraoperative management of hyperglycemia? Acta Anaesthesiologica Taiwanica. 2011;49(2):41-5.
27. Zerr KJ, Furnary AP, Grunkemeier GL, Bookin S, Kanhere V, Starr A. Glucose control lowers the risk of wound infection in diabetics after open heart operations. The Annals of thoracic surgery. 1997;63(2):356-61.
28. Hruska LA, Smith JM, Hendy MP, Fritz VL, McAdams S. Continuous insulin infusion reduces infectious complications in diabetics following coronary surgery. Journal of cardiac surgery. 2005;20(5):403-7.
29. Furnary AP, Zerr KJ, Grunkemeier GL, Starr A. Continuous intravenous insulin infusion reduces the incidence of deep sternal wound infection in diabetic patients after cardiac surgical procedures. The Annals of thoracic surgery. 1999;67(2):352-60.
30. Kramer R, Groom R, Weldner D, Gallant P, Heyl B, Knapp R, et al. Glycemic control and reduction of deep sternal wound infection rates: a multidisciplinary approach. Archives of Surgery. 2008;143(5):451-6.

Source of support: Shiraz anesthesiology and critical care research center. Proposal No 91-01-60-5268 and IRCT2013041713052N1, **Iran, Conflict of interest: None**