Prevalence and intensity of hyperglycemia in non-diabetic patients undergoing coronary artery bypass graft surgery with and without cardiopulmonary bypass

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ABSTRACT

الأهداف: دراسة انتشار وشدة ارتفاع سكر الدم لدى المرضى غير المصابين بداء السكري والخاضعين لعملية في القلب.

الطريقة: أجريت دراسة تطلعية شملت 282 مريضاً غير مصاب بالسكري خضعوا لعملية اختيارية بدون مضخة (عدد=101)، أو باستعمال المضخة (عدد=181) لتركيب مجازة للشريان التاجي (CABG). أجريت هذه الدراسة خلال الفترة من مارس 2006م وحتى يوليو 2007م، بمستشفى مداني – تابريز – إيران. قِيسَ مستوى سكر الدم (BG) خلال العملية وبعد 24 ساعة مِنها. تمت مقارنة تكرار ارتفاع سكر الدم (BG≥ 126 mg/dl)، وارتفاع سكر الدم الشديد (BG≥ 180 mg/dl) والمضاعفات بعد العملية الجراحية لدى مجموعتي الدراسة.

النتائج: بلغت نسبة الشيوع على الأقل لعارضة واحدة من ارتفاع سكر الدم الشديد (54.6%) (154/282) في مرضانا خلال العملية الجراحية وبعد 24 ساعة منها. ارتفاع سكر الدم أثناء العملية الجراحية كان أعلى بشكل بسيط في المجموعة التي استُخدمت لها المضخة. تكرار حدوث ارتفاع سكر الدم بعد العملية كان أعلى ولكن لم يكن هنالك فرقاً ملحوظاً بين المجموعتين،. لم يكن هنالك فرقاً ملحوظاً بين مجموعتي الدراسة ف ي تكرار حدوث ارتفاع سكر الدم الشديد أثناء العملية الجراحية، ، ولكن كان هنالك فرقاً خلال 24 ساعة بعد العملية.

خاتمة: كان انتشار سكر الدم، خاصة ارتفاع سكر الدم الشديد عالياً أثناء وبعد إجراء العملية الجراحية في كلتا المجموعتين التي استعملت المضخة والتي لم يتم استعمالها في عملية تركيب مجازة للشريان التاجي (CABG) لدى المرضى غير المصابين بداء السكري. كان هنالك فرقاً على الحدود في مستويات سكر الدم بين المرضى الذين أجريت لهم عملية تركيب المجازة للشريان التاجي (CABG) سواء استعملت لديهم المضخة أم لا. قد يكون من الحكمة الأخذ بعين الاعتبار طريقة التحكم بسكر الدم لدى هؤلاء المرضى خاصة في الفترة المبكرة بعد العملية الجراحية.

Objective: To study the prevalence and severity of hyperglycemia in nondiabetic patients undergoing cardiac operation.

Methods: In an observational prospective study, 282 non-diabetic patients underwent elective off-pump (n= 101) or on-pump (n= 181) coronary artery bypass grafting (CABG) surgery from March 2006 to July 2007 in Madani Heart Hospital, Tabriz, Iran. Blood glucose (BG) levels were measured during and 24 hours after operation. Frequencies of hyperglycemia (BG≥126 mg/dl) and severe hyperglycemia (BG≥180 mg/dl) and postoperative complications were compared in the 2 study groups.

Results: Prevalence of at least one episode of severe hyperglycemia was 54.6% (154/282) in our patients during, and 24 hours after operation. Intra-operative hyperglycemia was slightly higher in on-pump group. Frequency of post-operative hyperglycemia was higher, although not significantly different between the 2 groups. The 2 study groups were not significantly different in frequency of severe hyperglycemia during operation, although were different within 24 hours postoperative period.

Conclusion: Prevalence of hyperglycemia especially severe hyperglycemia was high during, and after operation in both off-pump and on-pump CABG in non-diabetic patients. There was a borderline difference in blood glucose level between on-pump and off-pump CABG patients. It may be prudent to consider glycemic control protocols in these patients especially in early post-operative period.

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Hyperglycemia is a well-known risk factor of cardiovascular death and perioperative morbidity and mortality in cardiac surgery patients.[1-4] However, most studies addressed the perioperative hyperglycemia in diabetic patients, or in all of the patients undergoing cardiac surgery irrespective of diabetes' mellitus status.[5-8] Some studies have shown that hyperglycemia in non-diabetic patients increases mortality after myocardial infarction and cardiac surgery.[8,9] However, we know little about exact prevalence of hyperglycemia in non-diabetic patients undergoing cardiac surgery. The aim of this study was to compare the prevalence and intensity of hyperglycemia in non-diabetic patients undergoing coronary artery bypass graft (CABG) surgery with and without cardiopulmonary bypass (CPB).

Methods. After approval from the Institutional Ethics Committee we conducted a prospective observational study. A total of 420 consecutive adult patients who underwent elective CABG surgery from March 2006 to July 2007 in Madani Heart Hospital, Tabriz, Iran were included in the study. Out of 420 patients, 138 patients were excluded from the study: 126 patients have diabetes mellitus, one patient died in the operating room, in 11 patients data collection was incomplete. Finally, 282 non-diabetic patients entered the study. The patients were divided into 2 groups: CABG without CPB or off-pump CABG group (n=101) as a study group, and CABG with CPB or on-pump CABG group (n=181) as a control group.

Baseline characteristics and surgical variables that might possibly be associated with hyperglycemia were collected in a common database. These variables included age, gender, body mass index, preoperative drugs (angiotensin converting enzyme inhibitors, calcium channel blockers, beta-blockers, and diuretics), left ventricle ejection fraction, CPB time, degree of hypothermia (in on-pump group), operation time, dopamine or dobutamine used more than 5 µg/kg/minute or intra-aortic ballone pump used, tracheal intubation time in intensive care unit (ICU), major postoperative complications, ICU and hospital stay time (**Table 1**).

Intraoperative arterial blood glucose levels (BG) were monitored simultaneously with arterial blood gas analysis with blood gas analyzer (GEM premier 3000, Instrumentation Laboratory, Lexington, USA). As the operating room routine protocol, BG levels measured 5 times in on-pump CABG, and 3 times in off-pump CABG operation. Postoperative arterial BG levels were monitored every 6 hours, and we recorded BG levels immediately after patient admission in ICU and at the sixth, twelfth, and twenty-fourth postoperative hours. Mean BG levels in each time was compared between the study groups. Frequencies of severe hyperglycemia (BG≥180 mg/dl), moderate hyperglycemia (BG= ≤150 to <180 mg/dl), mild hyperglycemia (BG= ≤110 to <150 mg/dl), normoglycemia (BG= ≤70 to <110 mg/dl), and hypoglycemia (BG<70 mg/dl) during and 24 hours after operation, compared between the groups (**Table 2**). We also compared postoperative adverse outcome frequencies between the 2 study groups.

Data analysis was performed using the SPSS for windows program package version 14.0 (SPSS Inc, Chicago, IL). Categorical variables were compared with the Chi-square or Fisher's exact test as appropriate with risk estimation [as odds ratio (OR) and 95% confidence interval (CI)]. Continuous variables analyzed with independent samples t-test. Mann-Whitney test was used as nonparametric test. All tests were 2 tailed, and a level of significance was set at $p \leq 0.05$.

Results. In this study, the prevalence of at least one episode of hyperglycemia (BG≥126 mg/dl) was 95%, and at least one episode of severe hyperglycemia (BG≥180 mg/dl) was 54.6% in non-diabetic patients undergoing CABG surgery (n=282). The 2 study groups appear to be comparable on all background characteristics except for inotrop/vasopressor administration in on-pump group (**Table 1**). Mean BG concentrations in different hours during operation and in early postoperative period are presented in **Figure 1**. There were no significant differences between the 2 groups in mean BG concentration in different hours during CABG. However, **Figure 1** shows that in on-pump group, mean BG concentrations was higher in sixth (180±49 versus 159±30 mg/dl, p=0.001) and twelfth hours (163±43 versus 153±27 mg/dl, p=0.033) of postoperative period.

Table 1 - Clinical characteristics of patients in off-pump and on-pump CABG groups.

Characteristics	Off-pump CABG* n=101	On-pump CABG* n=181
Age (years)	56.8 ± 10.4†	58.9 ± 9.6
Gender: Male/Female	79/78	145/80
BMI	28.4 ± 4.6	27.6 ± 4.1
Hematocrit (%)	41.7 ± 3.6	41.2 ± 4.4
Creatinine (mg/dl)	1.04 ± 0.24	1.04 ± 0.25
LVEF (%)	47.7 ± 8.8	49.8 ± 9.3
ACEIs	41 (40.6)	79 (43.6)
Calcium channel blockers	32 (31.6)	52 (28.7)
Beta-blockers	55 (54.4)	108 (59.6)
Diuretics	26 (25.7)	50 (27.6)
Operation time (min)	287 ± 68	319 ± 63
Inotrop/vasopressor administration	2 (3.9)	26 (14)
Intra aortic balloon pump	0	2 (1.1)

* CABG - coronary artery bypass graft surgery
† Values are shown as mean±standard deviation or no. (%).
BMI - body mass index
LVEF - left ventricle ejection fraction
ACEIs - angiotensin converting enzyme inhibitors

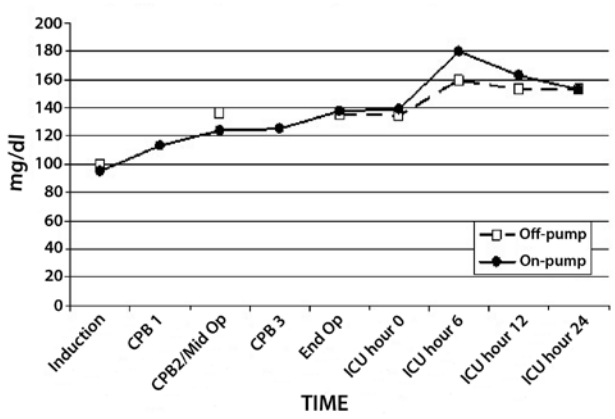

Figure 1 - Variation of blood glucose in off-pump and on-pump CABG patients during and after operation. CABG - coronary artery bypass graft surgery, CPB - cardiopulmonary bypass, ICU-Intensive Care Unit, Mid Op - middle of operation, End Op - end of operation (sternum closure)

Frequency of hyperglycemia (BG mg/dl) and its classified values in mild, moderate, and severe for the both groups are shown in **Table 2**. The incidence of intra-operative hyperglycemia is slightly higher in on-pump group, while there was no significant difference between the 2 groups in postoperative hyperglycemia. In this study hypoglycemia (BG<70 mg/dl) occurred only one time in one patient in off-pump group during operation, and in one another in on-pump group after operation. Finally as illustrated in **Table 3**, there were no significant differences in morbidity and mortality rate in non-diabetic patients with or without severe hyperglycemia (intra-operative and post-operative), except more post-operative cardiac and renal complications in patients who experienced severe hyperglycemia.

Table 2 - Prevalence and severity of hyperglycemia in non-diabetic patients with off-pump and on-pump CABG surgery.

Severity of hyperglycemia	Off-pump CABG	On-pump CABG	OR (95% CI)	*P*-value
	n (%)			
Intraoperative period:	n=101	n=181		
*Hyperglycemia**	53 (52.5)	118 (65.2)	1.70 (1.03-2.79)	0.049
Severe hyperglycemia†	12 (11.9)	34 (18.8)	1.72 (0.85-3.48)	0.181
Moderate hyperglycemia‡	18 (17.8)	31 (17.1)	0.95 (0.50-1.81)	1.000
Mild hyperglycemia§	23 (22.8)	53 (29.3)	1.40 (0.80-2.47)	0.298
Postoperative period:	n=100	n=172		
*Hyperglycemia**	89 (88)	160 (88.4)	1.65 (0.70-3.90)	0.356
Severe hyperglycemia†	25 (25)	71 (39.2)	2.1 (1.22-3.64)	0.010
Moderate hyperglycemia‡	34 (33.7)	53 (29.3)	0.86 (0.51-1.46)	0.683
Mild hyperglycemia§	30 (29.7)	36 (19.9)	0.62 (0.35-1.62)	0.125

*(BG ≥126 mg/dl), †(BG ≥180 mg/dl), ‡(150≤ BG <179 mg/dl), §(126≤ BG <149 mg/dl), CABG - coronary artery bypass graft surgery, OR - odds ratio, CI - confidence interval

Table 3 - Frequency of postoperative complications in non-diabetic patients with and without perioperative severe hyperglycemia.

Complications	Severe hyperglycemia		OR (95% CI)	*P*-value
	No (n=128)	Yes (n=154)		
Cardiac	18 (14.1)	37 (24)	1.9 (1.02-3.5)	0.044
Neurologic	2 (1.6)	5 (3.6)	2.0 (0.4-10.7)	0.467
Renal: (Cr* rise >50%)	5 (4)	16 (10.4)	3.2 (1.1-9.1)	0.040
Infectious	2 (1.6)	1 (0.6)	0.4 (0.04-4.5)	0.589
Long ventilation: (>18 hour)	8 (6.3)	12 (7.8)	1.1 (0.4-2.9)	0.969
Postoperative: bleeding >1000cc	17 (13.3)	14 (10)	0.6 (0.3-1.3)	0.306
Mortality	1 (0.8)	0	--	0.926

*Cr - creatinine, OR - odds ratio, CI - confidence interval

Discussion. Many studies show that hyperglycemia leads to metabolic alternations, impaired wound healing, exacerbation of ischemic brain injury, increased risk of infection, susceptibility to renal failure, and increased morbidity and mortality.[8-10] Due to the established adverse effects of hyperglycemia we studied the hyperglycemia as a surrogate adverse outcome, and did not include the complications of hyperglycemia in our study. Several studies have reported an increased perioperative morbidity and mortality in the patients with diabetes mellitus (DM), however, there are limited studies evaluating the frequency of complications during and after cardiac surgery in nondiabetic patients.

There were 3 major findings in our study: The first finding was very high prevalence of hyperglycemia - BG≥126 mg/dl- (95.0%), and severe hyperglycemia - BG≥180 mg/dl- (54.6%) in non-diabetic patients undergoing CABG surgery. The second finding was higher prevalence of hyperglycemia in early post-operative period than intra-operative period, and ascending trend of mean BG concentration from the beginning of operation until the twelfth post-operative hour (**Figure 1**). The third finding was that there was a little and borderline difference in prevalence and intensity of hyperglycemia in patients undergoing CABG using CBP in comparison with off-pump CABG patients (**Table 2**). Hyperglycemia is a frequent observation during acute illness such as myocardial infarction and after cardiac surgery. Hiesmayr[8] reported the frequency of hyperglycemia up to 95-100% after cardiac surgery (in both DM and non-DM patients). Smith et al[11] found that hyperglycemia (BG>144 mg/dl) occurs in 73% of non-DM patients following renal transplant surgery. Puskas et al[12] reported the incidence of hyperglycemia (BG>200 mg/dl) in non-DM (72%) versus in DM (83%) patients after on-pump CABG. While Estrada et al,[13] showed the prevalence of hyperglycemia (BG>150 mg/dl) in 51.5% non-DM and in 90.4% DM patients undergoing CABG. Prasad et al[14] emphasized on excessive and persistent BG elevation during cardiac surgery in non-diabetic patients with BG≥200 mg/dl in 70% of patients. Regarding the different definitions of hyperglycemia, our finding of prevalence of severe hyperglycemia - [BG≥180 mg/dl (54.6%)] in non-diabetic patients is comparable to the above mentioned studies' results. We assume that increasing pattern of hyperglycemia from intra-operative period to post-operative period was due to highly significant stress response to awakening from anesthesia in early post-operative period. Werb et al[15] reported this pattern as one of mechanisms of hyperglycemia in CABG surgery patients.

There was a borderline difference in BG level during operation between on-pump and off-pump CABG patients, this difference disappeared in post-operative period (**Table 2**). We did not find any published controlled study that compares hyperglycemia between on-pump and off-pump CABG surgery in non-diabetics, although, there are some evidence comparing hypothermic and normothermic cardiopulmonary bypass. For example, Lehot et al[16] showed that in non-diabetics BG level was not significantly different between hypothermic (25°C) and normothermic patients during CPB. Blood glucose level was higher in hypo- than normothermic CPB at closure of the chest (208 ± 30 versus 175 ± 19 mg/dl) and at the third post-operative hour (271 ± 30 versus 221 ± 51 mg/dl). Blood glucose values in this study emphasized the high prevalence of severe hyperglycemia and the ascending pattern of BG level from anesthesia induction to post-operative period in non-diabetic patients undergoing CABG.[16] In **Table 3**, it shows that only cardiac and renal complications were higher in patients with severe hyperglycemia (BG≥180 mg/dl), and there were no significant differences in other post-operative complications. However, samples size of this study is too small to evaluate the effect of severe hyperglycemia on post-operative morbidity and mortality.

In conclusion, the prevalence of hyperglycemia especially severe hyperglycemia was high during and very high after operation in both off-pump and on-pump CABG in non-diabetic patients. There was a borderline difference in BG level between on-pump and off-pump CABG patients. It may be prudent to consider glycemic control protocols in these patients especially in early post-operative period.

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References

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