Perioperative hyperglycemia: a strong predictor for atrial fibrillation after coronary artery bypass grafting surgery

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Context

Atrial fibrillation is the most frequent arrhythmia following cardiac surgery. Many risk factors for this problem have been studied.

Aims

The objective was to investigate the relation between perioperative hyperglycemia and postoperative atrial fibrillation (POAF) after coronary artery bypass grafting. Settings and design The study was a retrospective observational study that took place at Benha University Hospital, which is a tertiary referral center.

Patients and methods

The study was conducted on 100 patients who were admitted for coronary artery bypass grafting. Patients were divided into two groups: group A included 50 patients who developed POAF and group B included 50 patients who did not.

Statistical analysis

Data were imported into Statistical Package for the Social Sciences (SPSS version 20.0) software for analysis. Qualitative data represented as number and percentage and tested by the χ^2-test. Quantitative data were represented by mean±SD and tested by *t*-test or Mann–Whitney.

Results

The authors have found that a history of diabetes mellitus, mean postoperative blood sugar (BS), and maximum postoperative BS levels were more significant ($P<0.05$) in group A. The mean BS cutoff level that predicted the occurrence of POAF was 193.7 mg/dl. The authors also have found that postoperative drainage volume was higher in group A than group B, with *P* less than 0.001.

Conclusions

The authors believe that a history of diabetes mellitus, postoperative BS levels, and postoperative drainage volume were significant risk factors for the occurrence of POAF.

Keywords:
atrial fibrillation, coronary artery bypass grafting, postoperative arrhythmia

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Introduction

Postoperative atrial fibrillation (POAF) is defined as the development of new-onset atrial fibrillation (AF) early after surgery. It has an incidence of 20–40% of POAF after coronary artery bypass grafting (CABG) surgery. It causes many early adverse effects like increased ICU hospital stays. Furthermore, POAF was also linked to mid-term and long-term morbidity and mortality [1,2].

The pathophysiological mechanisms responsible for the occurrence of AF after cardiac surgery remain unclear. Recently, it was reported that metabolic diseases, including diabetes mellitus (DM), are related to AF occurrence [3,4].

Patients and methods

This retrospective observational study reviewed 100 patients who were admitted after CABG to the cardiac surgery intensive care unit. Ethics approval of the study protocol was approved by the Ethical Committee of the Faculty of Medicine at Benha University. Patients were divided into two groups: group A included 50 patients who developed POAF and group B included 50 patients who did not. We included patients who underwent isolated elective CABG, and their rhythm was sinus before admission. We excluded any patients who had valvular or congenital heart diseases. We also excluded any patient who had a history of AF, cardiac surgery, and hepatics or renal impairment. Patients were observed postoperatively, and arrhythmia data were recorded using a 12-lead ECG

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during ventilation, after weaning, and after removing chest tubes until discharge from the ICU.

Serum blood sugar (BS) was recorded every hour in the first six hours after surgery and then every 6 h. This was continued until discharge from the ICU. The maximum postoperative BS was defined as the highest level recorded from day zero to discharge, and mean BS was defined as the mean value of the BS measurements.

Other postoperative routine morning laboratory parameters were recorded like glomerular filtration rate (GFR), complete blood count, maximum creatine kinase-MB level, maximum and minimum K+ and Na+ levels, aspartate aminotransferase, alanine aminotransferase, and lactate levels.

We have compared the two groups according to patients' preoperative data (medical history, GFR, preoperative fasting BS level, and preoperative heart rate and blood pressure, echo findings) and postoperative data (cross-clamping time, bypass time, ventilation time, ICU stay time, drainage volume, blood transfusion, routine laboratory examinations, mean BS, maximum BS, and GFR).

Sample size calculation and statistical analysis

MedCalc software version 16.1 (1993–2016, MedCalc Software, MedCalc Software Ltd., Acacialaan, Ostend, Belgium) was used to calculate the required sample size using the percentage of AF (35%) according to Greenberg *et al*. [1]. The following variables were entered: level of significance (type I error)=0.05, type II error (1-level of power)=0.2, and prevalence of AF=35%. Null hypothesis percentage was 50% So, the least sample size required was 85 patients undergoing CABG. It was increased to 100 for more accuracy and divided into two groups (with AF and without AF, 50 patients each).

Data were imported into Statistical Package for the Social Sciences version 20.0 software (International Business Machines Corporation (IBM), Armonk, New York, USA) for analysis. Qualitative data were represented as number and percentage and quantitative continuous group was represented by mean±SD. The difference and association of the qualitative variables were tested by the χ^2 test. Differences between quantitative independent groups were tested by *t*-test or Mann–Whitney and paired by significance level. The *P* value was set at less than 0.05 for significant results and less than 0.001 for highly significant results.

Results

There were no significant differences ($P>0.05$) between both groups regarding age, sex, preoperative heart rate, and blood pressure (systolic and diastolic), and medical history regarding smoking and hypertension, but the history of DM was significant in group A ($P<0.001$), as shown in Table 1.

The preoperative echo findings were not statistically significant ($P=0.563$). The left atrium (LA) was dilated in 15 (30%) patients in group A versus 11 (22%) in group B, and the left ventricle (LV) was dilated with low EF in nine (18%) patients in group A in contrast to six (12%) patients in group B. The postoperative ejection fraction in group A was normal (>50%) in 26 (52%) patients and impaired

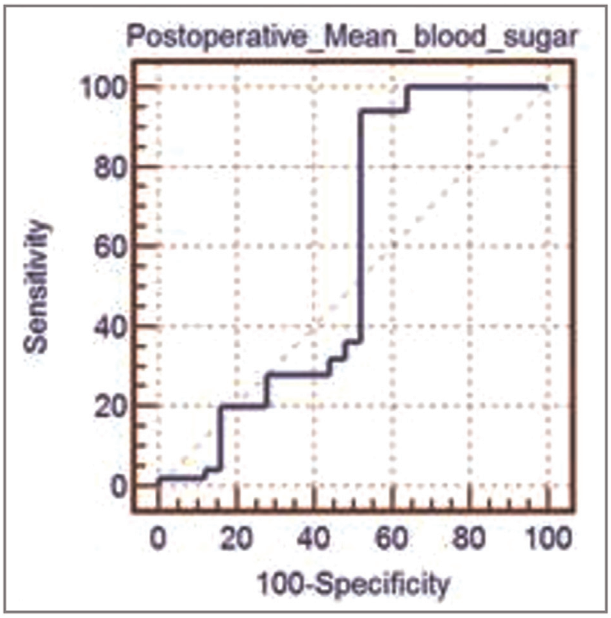
Table 1 Comparison between the two groups' demographics and clinical parameters

	Group A (*n*=50)	Group B (*n*=50)	*t* or χ^2	*P* value
Age				
Range	31–70	44–69	0.599	0.551
Mean±SD	58.36±10.33	59.44±7.47		
Sex [*n* (%)]				
Female	8 (16)	12 (24)	1.000	0.317
Male	42 (84)	38 (76)		
Medical history [*n* (%)]				
Smoking	41 (82)	45 (90)	1.329	0.249
Diabetes mellitus	36 (72)	15 (30)	17.647	<0.001
Hypertension	27 (54)	20 (40)	1.967	0.161
Preoperative heart rate (beats/min)				
Mean±SD	85.60±9.62	84.48±8.99	0.602	0.549
Diastolic blood pressure (mmHg)				
Mean±SD	86.60±14.23	87.20±14.00	0.213	0.832
Systolic blood pressure (mmHg)				
Mean±SD	131.80±20.77	133.40±20.06	0.392	0.696

Table 2 Comparison between the two groups' pre and postoperative blood sugar levels

Blood sugar level (mg/dl)	Mean±SD		t	P value
	Group A (n=50)	Group B (n=50)		
Preoperative fasting blood sugar	135.12±18.8	122.16±20.49	1.790	0.077
Postoperative mean blood sugar	206.68±53.65	187.88±27.81	2.200	0.030
Postoperative maximum blood sugar	277.37±58.91	255.00±47.01	2.098	0.038

Figure 1



Receiver operating characteristic curve between group A and group B regarding postoperative mean blood sugar (mg/dl).

(<50%) in 24 (48%) patients, whereas in group B, 22 (44%) patients had normal EF and 28 (56%) had impaired EF, with P value 0.702 between both groups.

There was no statistically significant difference (P>0.05) between the two groups regarding the preoperative fasting BS level. Postoperative mean and maximum BS level showed a statistically significant difference between the two groups (P<0.05), which was higher in group A, as shown in Table 2.

The receiver operating characteristic curve showed the best cutoff point is less than or equal to 193.7 mg/dl, with a sensitivity of 94%, a specificity of 48%, a positive predictive value of 64.4%, and a negative predictive value of 88.9%. We have assumed that patient with a mean BS more than 193.7 mg/dl is considered a positive risk factor for AF occurrence, as shown in Fig. 1.

There was no statistically significant difference (P>0.05) between the two groups regarding bypass time, cross-clamp time, ventilation time, ICU stay time, blood product transfusion, postoperative fluid balance, and presence of intra-aortic balloon. There was a statistically significant difference between the two groups regarding postoperative drainage volume (P<0.001), which was higher in group A than group B, as shown in Table 3.

There was no statistically significant difference (P>0.05) between the two groups regarding minimal and maximum hemoglobin levels, total leukocytic count, platelet count, maximum creatine kinase-MB level, minimal and maximum K+ and Na+, lactate, alanine aminotransferase, and aspartate aminotransferase levels, as shown in Table 4.

Discussion

In this study, a postoperative BS of less than 193.7 mg/dl was independently associated with lower incidence of POAF. Although the best cutoff remains controversial, Tatsuishi *et al.* [5], reported BS cutoff of less than 180 mg/dl predicts POAF. Others have reported that controlling BS to less than 200 mg/dl is beneficial. Furthermore, using tight glycemic control, such as reducing BS to less than 140 mg/dl, improves the early morbidity and mortality, especially those related to infections and ischemic events [6]. However, owing to the risk of hypoglycemia with such tight control [7], the guidelines from the Society of Thoracic Surgeons recommend mean BS of less than or equal to 180 mg/dl [8].

According to Tatsuishi *et al.* [5] and Ismail *et al.* [9], age was identified as an independent risk factor for POAF, which could be attributed to age-related co-morbidities. This has been explained by Amar *et al.* [10], who believed that degenerative changes occurring in the atrium by aging are sufficient to cause this type of arrhythmia.

We have found that the percentage of patients having a history of DM was 72% in group A compared with 30% in group B (P<0.001). This highly significant difference was similar to findings of Ismail *et al.* and Omer *et al.* [9,11].

Table 3 Comparison between the two groups regarding operative and postoperative data

	Group A (*n*=50)	Group B (*n*=50)	*t* or χ^2	*P* value
Bypass time (min)				
Range	60–140	60–140	0.117	0.907
Mean±SD	90±25.39	89.4±25.75		
Cross-clamping time (min)				
Range	30–110	30–105	1.318	0.191
Mean±SD	48.1±24.01	54.4±23.79		
Ventilation time (h)				
Range	6–35	6–47	0.926	0.357
Mean±SD	12±6.66	13.56±9.88		
ICU stay time (days)				
Range	2–6	2–6	1.523	0.131
Mean±SD	3.1±1.45	2.72±1.01		
Blood product transfusion [*n* (%)]				
Fresh blood	32 (64)	36 (72)	0.735	0.391
Packed RBCs	36 (72)	40 (80)	0.877	0.349
Plasma	37 (74)	41 (82)	0.932	0.334
Postoperative volume balance [*n* (%)]				
Positive	5 (10)	4 (8)	0.122	0.727
Negative	45 (90)	46 (92)		
Postoperative drainage volume (ml) [*n* (%)]				
Range	500–1800	400–1200	6.118	<0.001
Mean±SD	1164±401.91	768±218.94		
Intra-aortic balloon pump [*n* (%)]				
Yes	9 (18)	5 (10)	1.329	0.249
No	41 (82)	45 (90)		

RBCs, red blood cells.

Table 4 Comparison between the two groups' routine postoperative laboratory parameters

	Mean±SD		*t*	*P* value
	Group A (*n*=50)	Group B (*n*=50)		
Minimal hemoglobin (g/dl)	9.44±0.66	9.51±0.80	0.531	0.597
Maximum hemoglobin (g/dl)	12.55±1.15	12.12±1.57	1.582	0.117
TLC count (×10^9/l)	19.10±5.52	19.08±4.89	0.019	0.985
Platelet count (×10^9/l)	149.96±47.22	143.44±44.85	0.708	0.481
Max CKMB	38.18±47.28	39.34±60.41	0.107	0.915
Minimal k level (mEq/l)	3.85±0.29	3.85±0.27	0.036	0.972
Maximum k level (mEq/l)	5.07±0.40	5.02±0.44	0.645	0.521
Minimal Na level (mEq/l)	140.50±3.19	141.04±2.40	0.957	0.341
Maximum Na level (mEq/l)	144.20±2.02	143.84±1.75	0.951	0.344
Minimal lactate level (mmol/l)	1.72±0.58	1.56±0.41	1.557	0.123
Maximum lactate level (mmol/l)	6.64±1.62	7.12±2.03	1.289	0.201
ALT (μl/l)	19.40±10.11	19.24±8.46	0.086	0.932
AST (μl/l)	19.52±7.07	18.76±4.77	0.630	0.530
GFR (ml/min)	77.30±14.46	77.64±14.54	0.117	0.907

ALT, alanine aminotransferase; AST, aspartate aminotransferase; KMB, creatine kinase-MB; GFR, glomerular filtration rate; TLC, total leukocytic count.

In the Framingham heart study, DM was identified as an independent risk factor for AF on the long-term follow-up. This was explained by different mechanisms, which included DM-related atrial fibrosis owing to exaggerated systemic and tissue level oxidative stress and dysfunction in the autonomic innervation of the cardiovascular system [12]. Furthermore, according to Erickson *et al.* [13], Ca^{2+}/calmodulin-dependent protein kinase II (CaMKII) is increased in the heart and brain of diabetic patients. In cardiac cells, increased glucose level significantly stimulates Ca^{2+} release by CaMKII-dependent activation of sarcoplasmic reticulum, which contributes to myocardial dysfunction and arrhythmia [14,15].

Furthermore, the postoperative mean BS showed statistical significance (*P*=0.030) between the two groups, and maximum BS also showed statistical significance between the two groups (*P*= 0.038). These results were supported by Tatsuishi *et al.* [5]. Moreover, they found a strong positive correlation between the maximum postoperative BS level and the timing of postoperative AF. This was explained by various studies that tried to detect the effect of hyperglycemia on different stages of the cardiac cycle. Hyperglycemia prolongs both the P-wave dispersion and corrected QT duration, which are considered risk factors for AF. These effects were referred to the dysfunction of human ether-a-go-go-related gene K +-channel [16–18].

The preoperative and postoperative GFR showed no statistically significant difference between the two groups (*P*=0.493 and 0.907, respectively). According to Tatsuishi *et al.* [5], the postoperative GFR was significantly different between the AF and the non-AF groups, with *P* value 0.032, but in multivariate analysis, risk factors for POAF showed no significant difference.

In contrast to these results, Abdel-Salam and Nammas [19] and Gorczyca *et al.* [20], have shown that impaired renal function is related to the development of AF after cardiac surgery. This could be explained by activation of the sympathetic nervous system owing to stimulation of intrarenal chemoreceptors and mechanoreceptors, which leads to increased sympathetic nerve activity to the heart [21].

There was a statistically significant difference between the two groups regarding postoperative drainage volume (*P*<0.001), which was higher in group A than group B. According to many authors, hypovolemia and low cardiac output were related to POAF. Moreover, the use of β-blockers in such patients to prevent or treat AF is usually postponed owing to their hemodynamic instability [5,9].The postoperative levels of K and Na showed no significant difference (*P*>0.05) between the two groups. This can be explained by the tendency to rapidly correct any electrolyte disturbance postoperatively. However, it is well established that electrolyte imbalance in the form of hypokalemia or hypomagnesemia is associated with an increased risk of POAF [5].

In our study, there was no significant difference between both groups regarding ventilation time and ICU stays (*P*>0.05). In contrast, results from other studies have shown a significant difference in ventilation time and ICU stay, which was explained as a result of arrhythmia, which necessitates more time for treatment and patient stabilization [9,19].

Although we did not find a significant difference between both groups regarding preoperative and postoperative LA dimensions and EF (*P*>0.05), the influence of depressed preoperative EF and enlarged left atrium on POAF has been demonstrated in several studies [9,22].

Study limitations

The study was retrospective with its drawbacks of patient selection and investigation biases. Another limitation is the short-term follow-up.

Conclusion

We advocate to intensively control BS before and after surgery to less than 193.7 mg/dl and also to prevent and manage any postoperative bleeding to make drainage volume as less as possible to reduce the risk of developing post-POAF.

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Conflicts of interest

There are no conflicts of interest.

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