Original Article

Evaluation of Dysrhythmias Following Transfusion After Coronary Artery Bypasses Grafting

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ABSTRACT

Background: Coronary artery bypass graft surgery (CABG) is a common surgical operation usually performed under cardiopulmonary bypass. Although the relationship between the transfusion of blood products during and after surgery with the incidence of arrhythmia has been studied, contradictory results have been achieved. In the current study, we investigated the correlation between blood products transfusion during and after surgery with the incidence of postoperative arrhythmia.

Method: Patients candidated for CABG were entered into the present cross-sectional study. The incidence of arrhythmia (supraventricular and ventricular, transient or permanent), history of medications and renal diseases, and transfusion of blood products during or after the operation were recorded and analyzed.

Results: Twenty-two (8.2%) patients experienced atrial fibrillation and 50 (18.7%) experienced premature ventricular contractions. The use of packed red blood cells in the operating room was inversely correlated with the odds of the incidence of at least one of the arrhythmias (OR = 0.5, 95% CI: 0.28 to 0.87; P = 0.015). The number of grafts, high blood pressure, duration of mechanical ventilation in the ICU, and the potassium level upon admission to the ICU were directly correlated with the incidence of arrhythmia. Moreover, the transfusion of platelets in the ICU and the use of cryoprecipitate in the operating room were inversely correlated with the incidence of atrial fibrillation (not all arrhythmias).

Conclusions: According to the findings of the present study, conditionings to maintain the normal hematocrit level and platelet count is associated with decreased odds of arrhythmia incidence during and after CABG. ***(Iranian Heart Journal 2018; 19(1):44-51)***

KEYWORDS: Blood transfusion, Coronary artery bypass grafting, Postoperative arrhythmia, Transfusion

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Postoperative arrhythmias such as atrial fibrillation (AF) have been known as common complications occurring in more than one-third of patients after coronary artery bypass graft surgery (CABG) and even might be associated with severe complications such as mortality among patients. [1] Several studies have been performed on the early diagnosis of postoperative arrhythmias among patients undergoing cardiac operations and their associated complications. Some of these investigations have reported that postoperative atrial fibrillation (POAF) is a benign and self-limiting phenomenon, whereas some other studies have shown that POAF might lead to high rates of mortality or morbidities among patients. Some investigators have concluded that postoperative arrhythmias can increase the risk of stroke among patients. [2]

Miceli and associates [3] reported a remarkable difference in the non-anemic compared with anemic cardiac surgery patients in the risk of postoperative AF (33% vs 36.7%; $P = 0.003$). Moreover, Manzano-Fernández [4] showed that anemia was a predictor of patients with AF undertaking percutaneous coronary artery stenting. On the other hand, Mirhosseini et al [5] in patients undergoing off-pump CABG concluded that preoperative anemia did not affect the incidence of AF and early complications and mortality. Thus, there are conflicting data about the relation between anemia (and transfusion) and postoperative arrhythmias such as AF.

In most of the previous studies, AF is defined as a postoperative arrhythmia among patients undergoing off-pump CABG. It is reported that between 5.5% and 57.5% of patients might have experiences of postoperative arrhythmias. [6] Although we know postoperative arrhythmias as a multifactorial phenomenon, myocardial ischemia and incomplete myocardial protection are reported in most of the earlier studies as the main causes of postoperative arrhythmias. [7] The present study was performed to assess the incidence rate of postoperative arrhythmias in coronary artery disease patients undergoing CABG.

METHOD

The present cross-sectional study was performed in order to assess the frequency of postoperative arrhythmias after CABG in a referral university hospital between March 2015 and March 2016. The study protocol was approved by the institutional ethical research committee in accordance with the Helsinki research ethic deceleration. In total, 268 patients who met our inclusion criteria—including cardiac surgery on cardiopulmonary bypassing (CPB), no history of AF or current arrhythmia management, CPB time between 60 and 120 minutes, nonuse of defibrillators, and no history of cardiac arrest during surgery—were included in the study. Via the convenient sampling method, the study samples were selected and included in the study. Informed consent was obtained from the whole study population before the commencement of the study. The study samples were examined at the time of referral to the hospital and after history taking and clinical examination, echocardiography was performed for all of the participants so as to confirm the primary diagnosis. Anesthesia induction and maintenance and the CPB managing protocol were the same in all of the patients.

Red blood cell and blood product transfusion during or after surgery were recorded in the study checklist. Postoperative arrhythmia (supraventricular and ventricular, transient or permanent) according to the diagnosis of the cardiologist was assessed among study patients and findings were recorded into the study checklist. Accordingly, the patients were divided into those with or without postoperative arrhythmias as the case and control groups, respectively.

Statistical Analysis

The statistical analyses were performed with IBM SPSS Statistics for Windows, version 20.0. (Armonk, NY, USA). The quantitative and qualitative variables are presented as means ± standard deviations (SDs) and frequencies/percentages, respectively. The frequencies of the study outcomes were compared between the study groups with odds ratios (OR) by using the χ^2 test. The quantitative variables were compared between the groups using the independent samples *t*-test. A *P* value equal to or less than 0.05 was assumed as statistically significant results. Logistic regression analysis was performed to determine the independent predictors of the study outcomes. All the study variables with a *P* value less than 0.2 in the univariate statistical analysis were entered into the regression model and all of the variables which remained in the regression model were reported as the independent predictors of postoperative arrhythmias among the study participants.

RESULTS

Of the 268 patients, there were 186 (69.4%) males. The mean age and mean weight of the patients were 61.7 ± 8.5 years and 72.9 ± 16.1 kg, respectively (Table 1). On average, 3.2 ± 0.1 conduits were grafted during the CABGs. Postoperative arrhythmias were seen in 60 (22.39%) patients. Within the study period, 60 patients had at least 1 postoperative arrhythmia and accordingly the patients were divided into arrhythmia and no-arrhythmia groups. The mean age had no significant difference between the arrhythmia group and the no-arrhythmia (control) group (64.4 ± 8.1 vs 61 ± 8.5 y; *P*=0.53). The incidence of postoperative arrhythmias among the study participants was not associated with gender (*P* = 0.39). The number of surgical grafts was similar between the 2 groups (3.2 ± 0.85 vs 3.5 ± 0.82; *P* = 0.12) (Table 1). The frequencies of hypertension and diabetes mellitus as well as the consumption of beta-blockers are summarized in Table 2.

Most of the patients had O blood type; A and B blood types had a similar distribution between the 2 groups. Additionally, the AB blood group had the lowest frequency among the study participants. The means of CPB time, aortic cross-clamp time, and operation time in the arrhythmia group were similar with those in the control group (*P* > 0.05). Only 8.2% of POAFs and 18.7% of premature ventricular contractions (PVCs) were seen as postoperative arrhythmias among the study participants. The mean time of mechanical ventilation was nonsignificantly higher in the case group than in the control group (1080 ± 856 vs 825 ± 325 min; *P* = 0.077). Among the inotrope drugs, epinephrine had the highest usage rate in the operating room (18.66%) and the ICU (20.90%). The details of the usage of the inotrope and anticoagulation drugs in the operating room and the ICU are presented in Table 3.

There were decreases in the serum level of hemoglobin, hematocrit, and platelet count before and after surgery and also at 24 and 48 hours after surgery. The details of the serum levels of hemoglobin, hematocrit, and other variables in the 2 study groups are presented in Table 4. The numbers of the units of transfused fresh frozen plasma (*P* = 0.005) and platelets (*P* = 0.01) were significantly higher in the arrhythmia group than in the control group in the ICU the but not during surgery (Table 5).

Table 1. Comparisons of the demographic variables between the case and control groups

Demographic Variable	Arrhythmia Group (n=60)	No Arrhythmia Group (n=208)	*P*
Age (y)	64.4 ±8.1	61 ±8.5	0.53
Sex (female)	26%	32%	0.39
Weight (kg)	72±13	73±16	0.73
Graft	3.5±0.82	3.2±0.85	0.12

Table 2. Comparisons of the demographic and medical disorders between the case and control groups

Study Variable		Arrhythmia Group (n=60)	No Arrhythmia Group (n=208)	*P*
Past medical history	Alcohol	6 (10%)	14 (6.7%)	0.41
	Smoking	12 (20%)	60 (28.8%)	0.19
	Addiction	10 (16.6%)	36 (17.3%)	0.74
	CVA	4 (6.6%)	12 (5.7%)	0.73
	Thyroid disorders	0 (0%)	2 (0.9%)	1
	Renal disorders	10 (16.6%)	32 (15.3%)	0.84
	Hypertension	30 (50%)	118 (56%)	0.37
	Diabetes mellitus	20 (33.3%)	110 (52%)	0.008
Drug usage	ACE inhibitor	0 (0%)	16 (7.6%)	0.027
	Beta-blockers	10 (16.6%)	52 (25%)	0.013
	Calcium-channel blockers	0 (0%)	18 (8.6%)	0.044
	Diuretics	2 (3.3%)	12 (5.7%)	0.742

CVA, Cerebrovascular accident; ACE, angiotensin-converting enzyme

Table 3. Comparisons of the inotrope drug and anticoagulant usage between the case and control groups

	Operating Room	ICU
Epinephrine	50 ± 18.7	56 ± 20.9
Noradrenalin	4 ± 1.5	4 ± 1.5
Dopamine	8 ± 3	8 ± 3
Milrinone	4 ± 1.5	6 ± 2
Dobutamine	6 ± 2.2	2 ± 0.7
Pack cells	0.68 ± 0.83	0.96 ± 1.3
Fresh frozen plasma	0.42 ± 0.96	0.48 ± 1
Platelet	0.44 ± 1	0.34 ± 0.91
Cryoprecipitate	0.05 ± 0.41	-
Transamine	0.02 ± 0.19	0.04 ± 0.23
PCC	0.02 ± 0.14	-
Aprotinin	-	-

ICU, Intensive care unit

Table 4. Comparison of the serum levels of hemoglobin, hematocrit, creatinine, platelets, and urea between the case and control groups before and after surgery

	Pre Operation	Post Operation	Post Operation (24 h)	Post Operation (48 h)
Hemoglobin	14.9 ± 1.9	10.2 ± 1.7	10.1 ± 1.35	9.8 ± 1.3
Hematocrit	38.7 ± 4.5	32.8 ± 4.4	32.7 ± 4.2	31.3 ± 4.4
Platelet	233000 ± 65800	177000 ± 4800	164000 ± 4000	-
BUN	20.3 ± 9.5	21 ± 8.5	22 ± 9.9	27 ± 1.6
Creatinine	1.07 ± 1.04	0.91 ± 0.42	1.03 ± 0.47	1.21 ± 0.86

BUN, Blood urea nitrogen

Regression Analysis

Our univariate analysis showed that the graft number, mechanical ventilation time in the ICU, and serum level of potassium at the ICU admission time had positive and packed red blood cell usage in the operating room had negative significant associations with the incidence of at least one of the postoperative arrhythmias. In the regression analysis for POAF, the packed red blood cell usage had no significant association with this type of cardiac arrhythmia and only the number of surgical grafts had a negative association with POAF. The transfusion of platelets in the ICU and cryoprecipitate in the operating room had a negative association with POAF. A past history

of renal disorders had a significant association with the development of AF. Furthermore, the presence of PVC had no association with the study variables and only had significant association with the mechanical ventilation time in the ICU (OR = 0.99, CI: 0.99 to 1.00; $P < 0.05$) (Table 6).

Table 5. Comparison of the usage of blood products between the case and control groups

	Arrhythmia Group (n=60)	No Arrhythmia Group (n=208)	*P*
Packed cell usage in the operating room	0.0	0.17±0.03	0.19
Fresh frozen plasma usage the operating room	0.92±0.40	0.99±0.44	0.77
Fresh frozen plasma usage in the ICU	1.14±0.83	0.70±0.21	0.005
Platelet usage in the operating room	1.18±0.57	0.70±0.21	0.35
Platelet usage in the ICU	1.35±0.83	0.70±0.21	0.01
Cryoprecipitate usage in the operating room	0.18±0.03	0.02±0.2	0.12
Transamine usage in the operating room	0.0	0.02±0.2	0.43
Transamine usage in the ICU	0.25±0.07	0.24±0.04	0.43

ICU, Intensive care unit

Table 6. Regression analysis for the determination of the independent variables of postoperative arrhythmias between the study patients

Study Variable	*P*	OR (95% CI)
Number of grafts	0.008	1.99 (1.19-3.44)
Blood pressure	00.032	2.26 (1.07-4.79)
Packed cell usage in the operating room	0.015	0.50 (0.28-0.87)
Mechanical ventilation time in the ICU	0.007	1.0 (1.0-1.01)
Potassium at the ICU entrance	0.004	2.50 (1.34-5.0)

ICU, Intensive care unit

DISCUSSION

In the current study, 268 patients underwent CABG and 60 (22.39%) of them experienced postoperative arrhythmias. We had AF only in 8.2% and PVC in 18.7% of the cases as postoperative arrhythmias among the study participants. In the regression analysis for POAF, the transfusion of packed red blood cells had no significant association with this type of cardiac arrhythmia and only the number of surgical grafts had a negative association with POAF. The transfusion of platelets in the ICU and cryoprecipitate during surgery had a negative association with the occurrence of POAF. Moreover, the incidence of PVC had no association with the study variables, with the exception of the mechanical ventilation time in the ICU.

POAF is one of the most frequent cardiac postoperative dysrhythmias and can present in up to 40% of patients. [8] AF can cause irregular ventricular rhythms, decreased end-diastolic volumes in the ventricles, and loss of the cardiac output. [9] It seems that inflammation and oxidative stress are associated with the pathophysiology of POAF. Although most cardiac dysrhythmias are safe, in some cases, they can cause severe complications such as cardiac arrest. On the other hand, cardiac arrest due to arrhythmias is known as one of the most common causes of sudden death—especially in emergent operations. [10] New-onset POAF is the most frequent postoperative arrhythmia and can occur on the second to fourth days after cardiac surgery; in addition, it can increase the length of hospital stay and therapeutic expenditures. [11] The incidence of AF among the general population is about 1.7%; this rate is increased among patients with older age and patients with atherosclerosis and amounts to 3.6%. [12] Higher rates of POAF among patients seem to occur on the second or third day after the surgical operation. [13] We found that POAF had a lower incidence rate among our patients, but our POAF rate was in an accepted range. Our study

patients were younger than those recruited in similar studies. Unfortunately, we succeeded in assessing the incidence rate of POAF only until 48 hours after surgery and we did not use Holter monitoring for postoperative arrhythmia assessment among our patients; consequently, our study data were based on ECG monitoring and the patients' medical records.

In our study, chiming in with previous reports, there were significant relationships between age, sex, diabetes mellitus, and usage of beta-blockers and the occurrence of POAF among the study participants. Some pathophysiological factors such as atrial hypertrophy, fibrosis, dilatation, pericarditis, ischemia around the surgery location, and autonomic nervous system imbalance have been previously suggested as the causes of POAF. [14] Further, some preoperative factors such as higher age, gender, [15] previous history of chronic heart failure, chronic obstructive pulmonary disorders, chronic renal failure, diabetes mellitus, [16] previous history of metabolic syndrome, obesity, [17] severe stenosis of the right coronary artery, and preoperative blood transfusion have been reported as the risk factors for preoperative POAF. [18]

In the present study, blood transfusion and blood products had no significant association with the PVC incidence and the use of platelets in the operating room and cryoprecipitate in the ICU had a significant negative association with the incidence of AF. It seems that blood transfusion can increase the likelihood of POAF by inducing the inflammatory system and elevating the serum level of inflammatory mediators. [18] Fontes et al [18] studied CABG patients and found that a higher rate of preoperative white blood cells was associated with a higher chance of new-onset AF. Sood et al [19] in their study on 550 patients reported that postoperative blood transfusion had a significant association with POAF among their study population. It seems that using platelet and cryoprecipitate can prevent hemorrhage, maintain effective hemostasis, and prevent blood pressure changes and thereby protect patients against postoperative dysrhythmias. [20] We conclude that the quality of packed red blood cells and their maintenance time are the main factors affecting the immune system's response to packed red blood cell transfusion and arrhythmia occurrence. It is likely that damage to red blood cells has a role in inducing immune response via the production of active oxygen species. [21] Ruffin et al [21] reported that using nonsteroidal anti-inflammatory drug decreased AF via the suppression of inflammation among their patients. In our study, although there was no significant association between blood product usage and POAF, packed red blood cell transfusion had a protective impact against POAF. It seems that increased hemoglobin concentration and oxygen carrying capacity may be able to reduce the occurrence of postoperative arrhythmias.

Several previous studies have assessed the causative and prognostic factors of POAF. In a study on patients with acute myocardial infarction without a previous history of arrhythmias, researchers found that the patients who received blood transfusion were susceptible to all new-onset dysrhythmias and this association was confirmed in the regression analysis after the removal of the role of confounder variables. [22] Age is reported as the main variable in the presence of dysrhythmia-related complications; nonetheless, other independent and controllable variables have yet to be fully investigated. [23] Most of the previous studies have focused on AF as the most frequent postoperative dysrhythmia and accordingly, male patients with older age, inflammation, and longer signal-averaged P-wave are at higher risk for AF after CABG. In another study, POAF had no significant association between the patients undergoing CABG with and without CPB. [24]

CONCLUSIONS

The findings of the present study are concordant with similar previous studies

regarding the incidence of postoperative arrhythmias and its relation to blood transfusion within and after surgery. It seems that blood conservation techniques such as autologous priming and ultrafiltration methods can better conserve the serum level of hemoglobin. Multicenter studies with higher sample sizes are, however, needed for the confirmation of the findings of the current study.

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