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Is there any relationship of postoperative atrial fibrillation with the use of blood products and postoperative hemoglobin levels in patients undergoing coronary artery bypass grafting?

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Abstract

The goal of this study was to assess the relationship of postoperative atrial fibrillation (AF) with the use of blood products and postoperative hemoglobin levels following coronary artery bypass grafting (CABG). Eighty patients undergoing isolated CABG from June 2013 to December 2013 in our institution were included in this study, and divided into two groups that contain 40 patients according to their postoperative blood hemoglobin levels in this prospective study. In Group 1 and 2, there were patients that whose postoperative hemoglobin levels were below 10 g/dL and above 10 g/dL, respectively. Groups were compared with each other according to the use of blood products and occurrence of AF, then the relationship between use of blood products and occurrence of AF was analyzed. Moreover, patients that occur postoperative AF and patients that do not occur postoperative AF were compared with each other; thus, risk factor analysis for postoperative AF were performed. Postoperative AF was observed in 12 (30%) patients in Group 1 (mean age: 62.0±9.6 years, 24 male) and 7 (17.5%) in Group 2 (mean age: 60.3±9.0 years, 27 male), but this difference was not found to be statistically significant. When patients that occurred AF and did not occur AF were compared, according to the number of patients that had received blood products, the patients that had occurred AF had received more blood products than the patients whom had not occurred AF although again this difference was not statistically significant. In risk factor analysis; advanced age, low ejection fraction, obesity and the non-use of preoperative beta blocker were found to be risk factors associated with postoperative AF. In accordance with this study, the use of blood products and postoperative hemoglobin levels do not have an important impact on AF that occurs in patients undergoing isolated CABG. However, further studies with larger patient series are needed to elucidate this relationship.

Keywords: Atrial fibrillation, blood transfusion, hemoglobin, coronary artery bypass grafting

Introduction

Atrial fibrillation (AF) is the most commonly observed dysrhythmia following coronary artery bypass grafting (CABG) surgery. Its incidence following CABG varies between 10% and 40% [1,2]. Although postoperative atrial fibrillation (POAF) is seen as a harmless problem, it is related to increased postoperative morbidity, mortality, and healthcare cost. POAF is accompanied with increased cerebrovascular accident, cardiac insufficiency and the decreased hemodynamic performance of left ventricle [3-5]. The etiology and risk factors of AF are still controversial. Although various risk factors are identified for AF in the literature, advanced age is the only common risk factor reported in all the literature [6,7]. The effects of the use of blood products and postoperative blood hemoglobin levels in the etiology of AF that occurs after CABG surgery are debated in recent years and continue to be debated. Although the relationship between the occurrence of AF and especially the use and transfusion of blood products is expressed in almost all studies [8-11], there are only few studies that do not indicate about this relationship [12,13].

The goal of this present study was to evaluate the relationship between the use of blood products and postoperative hemoglobin levels and AF that occurs in patients that were performed CABG for coronary artery disease (CAD).

Material and Methods

Ethical Declaration

The study protocol was approved by the local ethics committee with the decision number of 2013-11/22 at the date of June 18, 2013. The study was conducted in accordance with the principles of the Declaration of Helsinki. All patients were informed about the study, and their informed consent forms were obtained before surgery.

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ınd Design

and December 2013, a total of 80 patients CABG for CAD in our institution were included of patients were collected, and prospectively tients were divided into two groups of 40 o their postoperative hemoglobin levels. They ose postoperative hemoglobin level was below 10 g/dl (Group 1) and whose postoperative hemoglobin level was 10 g/dl and above 10 g/dl (Group 2) during their postoperative follow-up. Exclusion criteria included patients who had a history of arrhythmia, patients who underwent emergency CABG, and patients who had redo cardiac surgery or additional surgery. Patients in both groups were compared with each other according to the use of blood products and the occurrence POAF and then the relationship between the use of blood products and the occurrence of AF was analyzed. By this means, risk factor analysis for POAF was performed and the postoperative follow-up results were compared. For this present study, POAF was defined as AF of any duration in the postoperative period, which requiring medical treatment (beta-blocker, calcium channel blocker, amiodarone, anticoagulants, etc.).

Surgical Approach

The surgical approach to be applied was planned a day before the surgery; nevertheless, the final decision regarding the surgical technique was made following the evaluation of coronary anatomy and ascending aorta during the surgery. In Group 1, in seventeen patients beating heart coronary bypass surgery technique without cardiopulmonary bypass (CPB), while twenty three patients conventional coronary bypass surgery technique with CPB was performed. In Group 2, in sixteen patients beating heart coronary bypass surgery technique, while twenty four patients conventional coronary bypass surgery was performed.

Postoperative Monitoring

All patients were transferred to the intensive care unit (ICU) after the operation. Patients were monitored continuously using a cardiac rhythm monitor during ICU follow-up. Daily routine electrocardiography (ECG) recording was taken from all patients during the hospital stay both in ICU and clinic. Additional ECG recording was taken if a patient complained clinical signs of arrhythmia such as palpitation. In ICU and clinical follow-up, the complete blood counts and hemoglobin levels of all patients that were controlled at least once in a day. Patients were transfused when the patients' hemoglobin levels < 8 g/dl or hematocrit value < 24%.

Statistical Analysis

All statistical analyses were conducted out using the Statistical Package for Social Sciences (SPSS) program (version 18.0, SPSS, Chicago, Illinois, USA). Whether the data were normally distributed or not was tested by Shapiro-Wilk test. While comparing the two groups; the independent sample t-test was applied for the variables that were distributed normally, and Mann-Whitney U test was applied for the variables that were not distributed normally. The variables that fit to the normal distribution were presented as mean ± standard deviation and for the variables that were not fit were presented as median, minimum and maximum values. For the categorical variables, the n and % values were presented and for the comparison, the test types applied to them were Pearson chi-square test, Freeman-Halton chi-square test and Fisher's exact test. A p value <0.05 was considered statistically significant.

Results

By the evaluation of the two groups which have 40 patients, POAF was observed in 12 (30%) and 7 (17.5%) patients in Group 1 (mean age 62.0±9.6 years, 29 male) and Group 2 (mean age 60.3±9.0 years, 32 male), respectively. However, comparing the two groups, no statistically significant difference was found (p>0.05).

In Group 1 to 36 patients (90%), and in Group 2 to 21 patients (52.5%) at least one unit of blood was transfused, and Group 1 was received a total amount of 81 units of blood transfusion, while Group 2 was received 46 units. In Group 1, 13 patients received 1 unit of blood transfusion, 8 patients received 2 units, 10 patients received 3 units, 4 patients received 4 units, and 1 patient received 6 units. In Group 2, 3 patients received 1 unit of blood transfusion, 11 patients received 2 units, and 7 patients received 3 units. Considering each group's amount of patients that received blood transfusion and the usage of total amount of blood transfusion units, it was appeared that the two groups have a significant statistical difference.

Demographic features and comorbidities of patients of each groups are shown in Table 1, and intraoperative data of patients are shown in Table 2. When comparing preoperative and intraoperative data of two groups; there were no statistically significant differences between two groups, and the groups were statistically similar. Postoperative data of patients are shown in Table 3. Among postoperative data of patients, according to lengths of ICU stay, lengths of hospital stay, decline in postoperative average hemoglobin level were statistically significant in terms of the number of patients in which blood product was used and the amount of total used blood product (p<0.05).

Table 1. Preoperative demographic features and comorbidities of patients

	Group 1	Group 2	P value
Age, years	62.0±9.6	60.3±9.0	0.425
Female / Male	11 / 29	8 / 32	0.599
LMCA disease	4 (10%)	3 (7.5%)	1.000
Hypertension	29 (72.5%)	21 (52.5%)	0.106
Hyperlipidemia	16 (40%)	19 (47.5%)	0.652
Diabetes mellitus	21 (52.5%)	15 (37.5%)	0.169
Smoking	20 (50%)	21 (52.5%)	1.000
Alcohol use	3 (7.5%)	3 (7.5%)	1.000
COPD	4 (10%)	7 (17.5%)	0.516
Carotid artery disease	10 (25%)	9 (22.5%)	1.000
Renal dysfunction	5 (12.5%)	4 (10%)	1.000
History of CVE	3 (7.5%)	3 (7.5%)	1.000
History of previous PCI	8 (20%)	7 (17.5%)	1.000
Ejection fraction < 50%	14 (35%)	9 (22.5%)	0.123
Obesity	11 (27.5%)	8 (20%)	0.599
Body mass index, kg/m2	27.8±3.9	26.8±3.8	0.241
Preoperative beta blocker use	25 (62.5%)	29 (72.5%)	0.474
Mean hemoglobin levels, g/dl	12.6±1.8	12.8±1.5	0.566

COPD: Chronic obstructive pulmonary disease, CVE: Cerebrovascular event, LMCA: Left main coronary artery, PTCA: Percutaneous coronary intervention

Table 2. Intraoperative data of patients

	Group 1	Group 2	P value
LITA use	40 (100%)	39 (97.5%)	1.000
Mean number of distal bypass	2.73±0.89	2.56±0.91	0.814
Aortic cross clamping time, minutes	56.0±11.5	59.5±11.9	0.352
Total CPB time, minutes	95±21.1	98±24.0	0.838
Total operation time, minutes	231.5±50.3	217.1±46.8	0.896

CPB: Cardiopulmonary bypass, LITA: Left internal thoracic artery

Table 3. Postoperative data of patients

	Group 1	Group 2	P value
Inotrope requirement	15 (37.5%)	11 (27.5%)	0.474
IABP requirement	1 (2.5%)	1 (2.5%)	1.000
Ventilation time, hours	8.0±2.6	7.2±2.4	0.155
Re-intubation	1 (2.5%)	0 (0%)	1.000
Cerebrovascular event	2 (5%)	0 (0%)	0.494
Wound infection	4 (10%)	2 (5%)	0.675
Pneumonia	1 (2.5%)	1 (2.5%)	1.000
Pneumothorax	0 (0%)	4 (10%)	0.116
Sternal dehiscence	2 (5%)	0 (0%)	0.494
Mediastinitis	0 (0%)	0 (0%)	>0.05
GIS complications	0 (0%)	1 (2.5%)	1.000
Renal dysfunction	5 (12.5%)	5 (12.5%)	1.000
Deep vein thrombosis	0 (0%)	0 (0%)	>0.05
POAF	12 (30%)	7 (17.5%)	0.293
Arrhythmias other than AF	11 (27.5%)	8 (20%)	0.599
Length of ICU stay, days	1.80±1.15	1.22±0.77	**0.010**
Length of hospital stay, days	7.37±4.15	5.80±2.65	**0.014**
Decline in mean hemoglobin levels, g/dl	5.25±1.68	2.71±1.41	**0.041**
Transfused patients	36 (90%)	21 (52.5%)	**0.001**
Total amount of used blood products, units	81	46	**0.001**
Mortality	1 (2.5%)	0 (0%)	1.000

AF: Atrial fibrillation, GIS: Gastrointestinal system, IABP: Intraaortic balloon pump, ICU: Intensive care unit, POAF: Postoperative atrial fibrillation

For the purpose of risk analysis of POAF, patients in which POAF occurred were compared with patients in whom POAF did not occur. Advanced age, low ejection fraction, obesity and the non-use of preoperative beta blockers were found to be statistically significant factors associated with POAF ($p<0.05$). In addition, ICU stay and the duration of hospital stay in patients in which POAF occurred were longer than patients in whom POAF did not occur. Data of patients with AF and non-AF postoperatively are shown in Table 4.

Table 4. Data of patients in whom POAF occurred and did not occur

	POAF(+) [n:19]	POAF(-) [n:61]	P value
Age, years	66.5±8.4	59.4±8.9	**0.003**
Female / Male	7 / 12	12 / 49	0.136
LMCA disease	2 (10.5%)	5 (8.2%)	0.668
Hypertension	12 (63.2%)	38 (62.3%)	1.000
Diabetes mellitus	11 (57.9%)	21 (34.4%)	0.120
Chronic obstructive pulmonary disease	5 (26.3%)	6 (9.8%)	0.120
Renal dysfunction	2 (10.5%)	8 (13.1%)	1.000
History of previous PCI	3 (15.8%)	12 (19.7%)	1.000
Ejection fraction <50%	10 (52.6%)	13 (21.3%)	**0.021**
Obesity	9 (47.4%)	10 (16.4%)	**0.011**
Body mass index, kg/m2	29.6±4.2	26.8±3.6	**0.029**
Preoperative beta blocker use	7 (36.8%)	47 (77%)	**0.003**
Ventilation time, hours	8.1±1.9	7.2±2.8	0.199
Inotrope requirement	8 (42.1%)	18 (29.5%)	0.457
IABP requirement	0 (0%)	1 (1.6%)	1.000
Transfused patients	16 (84.2%)	41 (67.2%)	0.255
Mean postoperative hemoglobin level, g/dl	9.77±1.35	10.48±1.44	0.066
Mean length of ICU stay [range], days	2 [1-5]	1 [1-4]	**0.008**
Mean length of hospital stay [range], days	7 [6-21]	5 [1-19]	**0.022**

IABP: Intraaortic balloon pump, ICU: Intensive care unit, LMCA: Left main coronary artery, POAF: Postoperative atrial fibrillation, PCI: Percutaneous coronary intervention

Discussion

Postoperative atrial fibrillation is one of the frequent complications following CABG. AF is a complication that increases mortality and morbidity because of stroke, heart failure, myocardial infarction (MI), thromboembolism, bleeding due to anticoagulation and re-hospitalization [3,14]. These patients require more treatment cost, drug use and nursing service. Therefore, it is important to prevent this cardiac arrythmia and develop optimal strategies for its treatment [15].

In early studies, POAF was defined as a temporary clinical condition, and there were insufficient knowledge about its short and long term effects. However, in more recent studies, effects of POAF on mortality and morbidity were evaluated extensively. It causes prolonged ICU and hospital stay, and leads to the problems for not only patients but also medical staff [14-16]. After cardiac surgery, AF usually occurs at postoperative 2nd and 3rd days. Although POAF is still considered as a ‘’benign phenomenon’’ from many surgeons, it can be also associated with increased cerebrovascular event (CVE), heart failure, and left ventricular hemodynamic performance decrease. After cardiac surgery,

patients that have AF have more CVE incidence than patients that do not during hospitalization [4]. AF may also cause hypotension and pulmonary edema. By returning the sinus rhythm, there is a significant recovery on cardiac index. In some studies, even though the level of disease is recovered, patients that have AF have more ICU stay and it is estimated that for each patient that has AF hospital spending is 10.000-11.000 American dollar [17,18].

In this study, we assessed the relationship between the use of blood products and postoperative hemoglobin levels and AF that occurs in patients who underwent CABG. In the literature, the first studies that show the relationship between AF and anemia were applied in 1970s. In a case report, it is shown that AF returns its normal sinus rhythm by blood transfusion to a patient that has AF and a serious anemia and by increasing hemoglobin levels [19]. In most of studies that evaluate the effect of blood hemoglobin levels on AF, it is observed that low hemoglobin levels, anemia, blood loss increase the rate of AF by doing sympathetic system activation. In a study performed by Houge and colleagues [20], it was shown that among risk factors of AF that occurs after cardiac surgery, there was also presence of postoperative anemia that increased the occurrence of reentry that is the mechanism of AF occurrence by the stimulation of sympathetic nervous system. In a study performed by Chelazzi and colleagues [21] that is a review on the occurrence of POAF, it was indicated that anemia, loss of blood and volume could play a role in the occurrence of AF by increasing sympathetic innervation and doing direct cardiac stimulation. However, in limited number of studies such as Auer and colleagues' study [13], and Ascione and colleagues' study [22], it was found that there was no significant impact of anemia, blood loss and low hemoglobin levels on the occurrence of AF after cardiac surgery. In this regard, the results of these two studies that evaluate the risk factors of AF that occurs after cardiac surgery show similarities with our study that evaluates the relationship between the occurrence of POAF and anemia and low hemoglobin levels.

In almost all studies in the literature, a significant relationship was determined between the occurrence of POAF and the use of blood products and transfusion. Namely, blood transfusion especially transfusion of erythrocyte suspension might strongly be associated with occurrence of POAF after cardiac surgery. In a study performed by Koch and colleagues [8] in which a total of 5841 patients underwent isolated CABG with or without valve replacement, it was found that blood transfusion was associated with the increased POAF risk. In a study performed by Sood and colleagues [10], erythrocyte transfusion in perioperative period was reported to be an important risk factor with a two-fold increase to occurrence of POAF. In a prospective study performed by Choi and colleagues [11] that included 315 off-pump CABG patients, it was similarly reported that erythrocyte transfusion was an important risk factor on the occurrence of POAF. Additionally, in the study performed by Straus and colleagues [23] in which CABG surgery was performed to 140 consecutive patients, and in another study performed by Topal and colleagues [24], it was found that blood product transfusion was the risk factor of POAF. In Gerber's study [9], in patients in which cardiac surgery was performed, the risk of blood transfusion was analyzed and the occurrence of AF is indicated as transfusion-related cardiac complication. In our study, at least one or more unit blood product was transfused to patients that had low level of postoperative hemoglobin (36 and 21 patients were transfused at least one or more unit blood in Group 1 and 2, respectively). In addition, the number of total blood product transfusion that was made to all patients in each group was much more in the group that has patients that have low hemoglobin level (Totally 81 and 46 units of blood product were transfused in Group 1 and 2, respectively). Between two groups, these differences of the number of patients in which blood products were used and total use of blood products were also statistically significant. Although we wanted to avoid the use of blood products as much as possible because of the avoidance of a possible transfusion reaction, it was apparent that this difference was higher in the group that has low hemoglobin level arises from the need to replace low hemoglobin levels. Additionally, when patients in which POAF occurs compared with in which POAF does not occur according to the number of patients in which blood products were used, at least one unit blood product was used in 84% (n:16/19) of patients in which POAF occurs and 67% (n:41/61) of patients in which POAF does not occur, but this difference was not found to be statistically significant. In only a limited number of studies, it was not demonstrated the clear relationship between the use of blood products and the occurrence of POAF. As in Murphy and colleagues' study [12], the impacts of the use of blood products in cardiac surgery patients were evaluated in terms of mortality, postoperative morbidity and cost, and it was not demonstrated the clear relationship between the use blood products and the occurrence of POAF. In also our study, the patients in whom POAF occurs were compared with the patients in whom POAF does not occur according to the use of blood products. Although the use of blood products was observed higher in the patients in whom POAF occurs, this difference was not found to be statistically significant. In this regard, our study was similar to this study.

Several risk factors that are responsible for the occurrence of POAF are defined in the literature. Within these, advanced age is strongest risk factor. Furthermore, some factors such as history of previous AF, low EF, high EuroSCORE score, chronic obstructive pulmonary disease, pulmonary hypertension, left atrial diameter, and prolonged mechanical ventilation time can be associated with the occurrence of POAF [25-27]. In also our study, the patients in which POAF occurs were compared with the patients in whom POAF does not occur and the analysis of risk factors was performed according to the occurrence of POAF. Advanced age, low EF, obesity, and not using preoperative beta blocker were found to be risk factors associated with occurrence of POAF. In addition, the lengths of ICU and hospital stay were longer in patients whom POAF occurs than the patients which POAF does not occur.

Main limitations of this present study were the small sample sizes in the groups and to be limited on evaluated data. Another important limitation was comparing the groups in off-pump and on-pump cases without subdividing them.

Conclusion

In accordance with this study, we deduced that there is no relationship of POAF with the use of blood products and postoperative hemoglobin levels in patients undergoing CABG. When all data are though of as together, more prolonged studies and broader patient participation are necessary to identify the reasons, risk factors, ways of protection and appropriate treatment strategies of POAF.

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Competing interests
The authors declare that they have no competing interest.

Financial Disclosure
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Ethical approval
The study protocol was approved by the local ethics committee with the decision number of 2013-11/22 at the date of June 18, 2013.

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