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Risk Factors of Red Blood Cell Transfusion in Isolate off Pump Coronary Artery Bypass Surgery

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Background: Perioperative transfusion of red blood cell (RBC) may cause adverse effects. Bloodless-cardiac surgery has been spotlighted to avoid those problems. Off pump coronary artery bypass (OPCAB) surgery can decrease the transfusion. However, the risk factors of transfusions in OPCAB have not been investigated properly. ***Materials and Methods:*** One hundred and thirteen patients (male:female=35:78, mean age=66.7±9.9 years) who received isolated OPCAB were retrospectively analyzed from March 2006 to September 2007. The threshold of RBC transfusion was 28.0% of hematocrit. Bilateral internal thoracic arteries graft were used for 99 patients (87.6%). One hundred and three (91.1%) and 35 patients (31.5%) took aspirin and clopidogrel just before surgery. ***Results:*** Sixty-five patients (47.5%) received the RBC transfusion (mean 2.2±3.2 units). Mortality and major complications were not different between transfusion and no-transfusion group. But, ventilator support time, intensive care unit stay and hospitalization period had been reduced in no-transfusion group ($p<0.05$). In multivariate analysis, patients risk factors for RBC transfusion were preoperative low hematocrit (<37.5%) and clopidogrel medication. Surgical risk factors were longer graft harvesting time (>75 minutes) and total operation time (>5.5 hours, $p<0.05$). ***Conclusion:*** We performed the transfusion according to transfusion guideline; over 40% cases could conduct the OPCAB without transfusion. There were no differences in major clinical results between transfusion and non-transfusion group. In addition, when used together with accurate understanding of transfusion risk factors, it is expected to increase the proportion of patients that do not undergo transfusions.

Key words: 1. Blood transfusion
2. Coronary artery bypass
3. Cardiopulmonary bypass

INTRODUCTION

Perioperative red blood cell (RBC) transfusion may increase the adverse effect such as acute hypersensitive reactions, coagulopathy, acute respiratory problems, and infections [1]. Particularly the increase of intraoperative blood transfusions in cardiac surgery can makes chances to meet the problems like postoperative renal failure, arrhythmia, and death [2-5]. In addition, lack of blood and the spread of religious and social hostility towards blood transfusions are leading to demands to minimize transfusions during cardiac surgery and active research is being conducted [5,6].

Off pump coronary artery bypass (OPCAB) can reduced the postoperative bleeding because there is no surgical in-

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cision in the heart, a small amount of heparin is used and there is little dilution of the coagulation factors. In addition, there is no diuretic effect and hemolysis that can be an adverse effect of cardiopulmonary bypass (CPB) [7-9]. We aim to analyze the clinical result of OPCAB between transfusion and non-transfusion group and the risk factors of RBC transfusions.

MATERIALS AND METHODS

Out of 127 OPCAB from March 2006 to September 2007, 113 patients, excluding the 14 patients who received other additional surgeries, were selected. The medical records of the 113 patients were reviewed in retrospect (male:female=78:35, mean age=66.7±9.9 years). The patients were divided into transfusion group and non-transfusion group according to whether they received RBC transfusions, and clinical result differences and changes of hematocrit were evaluated. The risk factors of RBC transfusions were analyzed, divided into patient factors and surgical factors.

RBC transfusions were only conducted in one of the followings. Hematocrit in the blood was under 28.0% (hemoglobin of 8.5 gm/dL) during or after surgery, hematocrit was under 30.0% (hemoglobin of 9.0 gm/dL) with chest tube drainage was 500 mL/hr or above after surgery, when changes in symptoms such as hypotension, tachycardia decrease urine output, due to bleeding. Fresh frozen plasma platelet concentration was used only in the abnormal results in coagulation test.

Analysis of clinical results, RBC transfusions risk factors was conducted using univariate analysis through two by two or two by Pearson's chi-square test, and multivariate study using logistic regression analysis. Changes in hematocrit of the two groups before and after surgery were compared using average comparison through t-test analyzed. Statistical significance was defined as p-value of 0.05 or less. The software used for analysis was SPSS ver. 18.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

1) Clinical results

The mean weight was 57.10±3.52 kg, mean body mass index (BMI) was 24.52±30.01. The average hematocrit before surgery was 38.10±5.47%. Sixty cases (50.1%) were emergency operation. The both internal thoracic artery (ITA) was used for the bypass graft in 99 cases (87.6%), left ITA was used in 9 cases (8.0%). The other vessels were used in 5 cases (4.4%) (Table 1). It took 90.45±35.06 minutes for mean graft harvesting, and the average number of distal anastomosis was 3.20±1.11. The mean operation time was 259.30±65.16 minutes other patients profile were listed in Table 1.

There were no deaths in any of the 113 cases included in this study. There were 46 cases of complications related to surgery (40.7%). Twenty-three of those cases (20.4%) were arrhythmia, 6 cases (5.3%) were neurological problems, and 4 cases (3.5%) were reoperation due to bleeding. There were 8 cases (7.1%) with other complications (cardiac arrest 2, respiratory problem 3, acute renal failure 2, and cholecystitis 1). But there were a higher proportion of overall complications in the transfusion group. The transfusion group also had significantly longer ventilator support time, intensive care unit admission duration, and hospitalization after surgery ($p<0.05$), but there were no differences between the two groups in mortality and major complications such as neurological problem, arrhythmia, or reoperations due to bleeding ($p>0.05$) (Table 2).

2) Red blood cell transfusions

Sixty-five cases of RBC transfusions (57.5%, mean 2.2±3.2 units) were conducted during the hospitalization. There were 27 cases of intraoperative transfusion (mean 0.52±1.23 units) and 55 cases of postoperative transfusion (mean 1.74±2.8 units). Seventeen (15.0%) of these cases transfused RBC both during and after surgery. There were only 18 cases (15.9%) of fresh frozen plasma and platelet transfusions.

Hematocrit increased with time for both groups after surgery (p=0.00), and there was no significant difference between the two groups from three days after surgery (p=0.17). The results of laboratory test when the patients visited the

Table 1. Patients profile

Profile	Results
Patient	
Mean age (yr)	66.7±9.9
Sex (male:female)	78:35
BMI (kg/m^2)[a)]	24.52±30.01
Diabetes mellitus	55/113 (48.6)
Hypertension	83/113 (73.5)
Renal failure[b)]	16/113 (14.2)
PCI history	11/113 (9.7)
Acute coronary syndrome[c)]	84/113 (74.3)
3 Vessel disease	95/113 (84.1)
Left main disease	30/113 (26.54)
Atrial fibrillation	1/113 (0.8)
Left ventricle dysfunction[d)]	1 (9.7)
Aspirin	103 (91.1)
Clopidogrel	35 (31.0)
Hematocrit	38.10±5.47
Operation	
Intra-aortic balloon pump	9 (8.0)
Emergent, urgent operation	60 (53.1)
Graft	
LITA＋RITA	75 (66.4)
LITA＋RITA＋SVG	24 (21.2)
LITA＋other vessel	6 (5.3)
LITA only	3 (2.7)
SVG only	3 (2.7)
Etc.	2 (1.7)
Anastomosis number	3.2±1.1
Harvesting time (min)	90.5±35.1
Operation time (min)	259.3±65.2
Intra-operation fluid intake (mL)	3.2±1.4

Values are presented as mean±standard deviation or number (%).
BMI, body mass index; PCI, percutaneous coronary intervention; LITA, left internal thoracic artery; RITA, right internal thoracic artery; SVG, saphenous vein graft.
[a)]Weight in kilograms by the square of their height in meters.
[b)]Chronic renal failure or increase creatinine over 50% of normal range.
[c)]Acute myocardial infarction＋unstable angina.
[d)]Ejection fraction ＜40%.

first outpatient department showed that the both groups maintained a high hematocrit concentration around 35% ($p<0.05$) (Table 3).

3) Analysis of risk factors of red blood cell transfusions

In order to find out the risk factors of increased RBC transfusions, the factors were divided into patient factors and surgical factors, and univariate and multivariate analyses were conducted.

(1) Analysis of patient factors: Patient factors related to increase of intraoperative, postoperative and total RBC transfusions during hospitalization were analyzed. Increased intraoperative RBC transfusions were found to be related to diabetes and low hematocrit before surgery in both univariate and multivariate studies ($p<0.05$) (Tables 4, 5). Postoperative RBC transfusions significantly increased the patient taking clopidogrel, low hematocrit before surgery and renal failure in both univariate and multivariate studies too ($p<0.05$) (Tables 4, 5). Taking clopidogrel, low hematocrit before surgery, light weight, and renal failure were found to be related total transfusion through univariate analysis ($p<0.05$). But results of the multivariate analysis only found that taking clopidogrel and low hematocrit before surgery were related to increased total RBC transfusions ($p<0.05$) (Tables 4, 5).

Table 2. Clinical results

Results	Transfusion	Non-transfusion	p-value
Mortality	0/65	0/48	1.000
Complication	32/65	14/48	0.032
Neurologic problem	3/65	3/48	0.428
Arrhythmia	13/65	5/48	0.169
Bleeding	1/48	3/62	0.472
Other problems	0/48	7/65	0.019
Ventilator support time (hr)	16.82±12.98	11.31±11.27	0.020
Intensive care unit stay (hr)	47.12±35.01	31.83±17.72	0.007
Admission (day)	11.64±8.44	7.02±2.42	0.000

Table 3. Postoperative hematocrit change

Time	Hematocrit (%)		p-value
	No transfusion	Transfusion	
Pre Op.	39.93±5.25	36.76±5.28	0.002
Post Op. #0	30.75±4.02	27.54±4.06	0.000
Post Op. #1	30.25±4.29	28.07±3.90	0.006
Post Op. #3	30.97±4.77	29.87±3.76	0.190
Post Op. #5	32.32±4.25	32.72±3.94	0.607
1st Opd. visit	35.40±4.18	34.56±4.06	0.290

Values are presented as mean±standard deviation.
Op, operation; Opd, out patients department.

Table 4. Univariate analysis of risk factors of red cell transfusion

Risk factor	p-value (odds ratio)		
	Total transfusion	Intra Op. transfusion	Post Op. transfusion
Patients factor			
Old age	0.600	0.063	0.277
Female sex	0.863	0.790	0.956
Low weight	0.214	0.011	0.027
Low BMI[a)]	0.175	0.129	0.241
Hypertension	0.933	0.712	0.237
Diabetes mellitus	0.010	0.109	0.097
Renal failure[b)]	0.168	0.008	0.038
Atrial fibrillation	1.000	0.496	0.242
PCI history	0.307	0.357	0.666
Acute coronary syndrome[c)]	0.131	0.274	0.681
3 Vessel disease	0.786	0.114	0.326
Left main disease	0.678	0.712	0.237
Left ventricle dysfunction[d)]	0.782	0.120	0.283
Aspirin	0.762	0.489	0.240
Clopidogrel	0.435	0.010	0.045
Low henatocrit	0.00	0.001	0.001
Surgical factor			
Intra-aortic balloon pump	0.132	0.310	0.200
Emergent, urgent Op.	0.039	0.920	0.571
Graft number	0.691	0.584	0.559
Intra operative fluid intake	0.016	0.021	0.013
Harvesting time	0.049	0.003	0.002
Op. time	0.009	0.044	0.003

Op, operation; BMI, body mass index; PCI, percutaneous coronary intervention.
[a)]Weight in kilograms by the square of their height in meters.
[b)]Chronic renal failure or increase creatinine over 50% of normal range.
[c)]Acute myocardial infarction + unstable angina.
[d)]Ejection fraction < 40%.

Table 5. Multivariate analysis of risk factors of red cell transfusion

Risk factor	Intraoperative transfusion	Postoperative transfusion	Total transfusion
	p-value (odds ratio)		
Patient factor			
Diabetes mellitus	0.012 (5.97)	0.627	0.704
Renal failure[a)]	0.968	0.050 (5.38)	0.074
Clopidogrel	0.551	0.002 (5.87)	0.007 (5.61)
Hematocrit (%)			
>43.0	0.001	0.109	0.003
37.5−43.5	0.454	0.257	0.195
31.5−37.5	0.107	0.039 (6.26)	0.003 (28.12)
≤31.5	0.002 (94.07)	0.034 (7.75)	0.001 (43.05)
Weight (kg)			
>75.0	0.382	0.260	0.463
60.0−75.0	0.199	0.105	0.133
45.0−60.0	0.376	0.046	0.116
≤45.0	0.847	0.999	0.999
Surgical factor			
Emergent, urgent operation	0.009 (7.89)	0.835	0.355
Intra operation fluid intake (mL)			
≤2,500	0.773	0.347	0.868
2,500−3,500	0.700	0.671	0.739
3,500−4,500	0.439	0.295	0.117
>4,500	0.319	0.353	0.873
Graft harvesting time (min)			
≤75	0.080	0.068	0.016
75−105	0.034 (7.63)	0.053	0.011 (6.40)
>105	0.049 (8.3)	0.036 (4.26)	0.014 (6.83)
Total operation time (hr)			
≤3.5	0.200	0.248	0.045
3.5−5.5	0.235	0.154	0.055
>5.5	0.076	0.107	0.012 (59.40)

[a)]Chronic renal failure or increase creatinine over 50% of normal range.

(2) Analysis of surgical factors: Surgical factors related to increase of intraoperative, postoperative and total RBC transfusions during hospitalization period were analyzed. Increased intraoperative RBC transfusions was related to emergency/urgent operation, amount of fluids infused during surgery, graft harvesting and total operation time through univariate analysis ($p<0.05$). But the multivariate analysis results showed that only emergency/urgent surgery and graft harvesting time influenced RBC transfusion ($p<0.05$) (Tables 4, 5).

Results of univariate analysis showed that amount of fluids infused during surgery, graft harvesting time and total operation time were related to postoperative RBC transfusions. But only the graft harvesting time was found to significant increased postoperative transfusions from the multivariate study ($p<0.05$) (Tables 4, 5).

Increased total RBC transfusions during hospitalization was related to graft harvesting time, operation time, and amount of fluids infused during operation in univariate analysis ($p < 0.05$). But multivariate analysis results only showed that graft harvesting and operation time increased total RBC transfusions during hospitalization ($p < 0.05$) (Tables 4, 5).

DISCUSSION

There have been many studies on the adverse effects of perioperative transfusions of cardiovascular patients over the years. Ferraris and Ferraris [3] demonstrated that transfusions increase renal failure, atrial fibrillation, infections, and respiratory problem and Hebert et al. [2] reported through the large-scale transfusion requirements in critical care study conducted in 1999 that transfusion increases the complications after cardiac surgery. Among two large randomized studies in 2004 and 2005, Vincent et al. [4] and Corwin et al. [5] evaluated that transfusion after cardiac surgery increases both mortality and complications. In order to reduce such complications methods such as using drugs like tranexamic acid, autologous transfusion before surgery and diluting blood are being used and studied [6,10,11] and application of autologous transfusion, retrograde autologous priming, and ultrafiltration are being conducted in Korea too [12-14].

There have been many studies in the past on the risk factors related to increased RBC transfusions during cardiac surgery. In 2007 the cardiac surgery transfusion guidelines, Society of Thoracic Surgeons Blood Conservation Guideline Task Force et al. [15] with cardiac surgeons and anesthetists reported that old age, anemia before surgery, low BMI, emergency surgery, open-heart surgery, anti-platelet agent, and coagulation abnormality were perioperative risk factors related to increased transfusions, and many other studies have presented similar results [7,8]. In Korea, Kim et al. [16] reported in 2000 that old age, left main disease, CPB support time, and albumin level before surgery were related to increased transfusions. In our study, risk factors for RBC transfusion were preoperative low hematocrit (<37.5%) and clopidogrel medication. Surgical, longer graft harvesting time (>75 minutes) and total operation time (>5.5 hours, $p < 0.05$).

Regarding surgical options, Despotis et al. [7] and Liu et al. [8] reported that coronary artery bypass surgery requires less RBC transfusions compared to open-hear surgery and Angelina et al. [17] reported in their randomized Beating Heart Against Cardiologic Arrest Studies and two meta-studies that OPCAB can further RBC transfusions [18].

There can be some debate about the guideline for transfusions during cardiac surgery. In this study, the RBC transfusion guideline in case of no bleeding was set as 28.0% of hematocrit. In 2007, Society of Thoracic Surgeons Blood Conservation Guideline Task Force et al. [15] presented the standard for transfusion in their transfusion guideline for cardiac surgery as hemoglobin of 6.5 gm/dL during surgery and 7.0 gm/dL after surgery, and the cardiovascular anesthetic standard of the American Society for Anesthesiologists is blood hemoglobin of 6.0 gm/dL for those under the age of 65, and 7.0 gm/dL for those who are 65 years of age or older [15]. In Korea, Kim et al. [14] presented a standard of hematocrit 15% when using a cardiovascular machine and 21% after surgery in 2009. Many domestic and international researchers as such as presenting a guideline (hemoglobin concentration of 6 to 8.5 gm/dL) that is lower than the general threshold for transfusion. This is based on the consideration of transfusion adverse effect, irrelevance between the survival rate of patients and hemoglobin concentration, research on minimum hemoglobin concentration for the maintenance of tissue oxygenation, and correlation with high hemoglobin concentration and graft occlusion [2,13,19].

In this study only 65 cases (57.5%) were conducted RBC transfusions during hospitalization. The number of intraoperative transfusions was especially only 27 cases (23.9%), indicating that many patients underwent surgery without a transfusion. However, postoperative transfusion was conducted for 38 of the 86 cases (44.2%), where there was no intraoperative transfusion. Transfusion during hospitalization is therefore expected to reduce even further through method such as careful hemostasis, autologous transfusion, using cell savers, active use of hemostatic drugs, and abiding by accurate transfusion guideline.

Patient factors that increased transfusions were examined. A low hematocrit before surgery increased transfusions during hospitalization with high odd ratio in multivariate analysis, and it was confirmed that hematocrit before surgery would become an index for predicting RBC transfusion. In addition, it appears as if RBC transfusions during hospitalization period can be reduced for some cases such as patients of renal failure and chronic anemia if hematocrit is increased using iron restraints or haemopoietic factors before surgery [13].

Taking clopidogrel during surgery does not affect intraoperative transfusions, but it was found to increase postoperative transfusions and finally it increases the transfusions during the hospitalization. Therefore, more careful hemostasis is required when operating on patients taking clopidogrel. However, it became clear that taking aspirin does not affect transfusions, so there is no reason to stop aspirin before surgery.

Diabetes was related to increased intraoperative transfusions, but it was not found to increase total transfusions. BMI, which was found to be significant in many studies [20], but did not have significance in this study, there was significance for light weight in univariate analysis only. This appears to be because of the height and weight of Koreans, who are comparatively smaller, and there should be future studies on this. Renal failure increase postoperative RBC transfusions and total transfusions in univariate study only. Further clinical observations and research are needed on transfusions of patients of renal failure after cardiac surgery (Tables 4, 5).

The results of the multivariate study showed that graft harvesting and operation time are surgical factors that increase total transfusions during hospitalization. Graft harvesting time especially had a high odd ratio on increase of both intraoperative and postoperative RBC transfusions based on a standard of 75 minutes, and operation time also had a high odd ratio when it was more than 5 hours 30 minutes. Therefore, efforts to minimize graft harvesting time and operation time are required to reduce transfusions. However, the number and type of graft and number of distal anastomosis is not related to red cell transfusions. The amount of fluids during surgery only showed positive results in univariate analysis, indicating that efforts to minimize fluid amount during surgery can lead to a decrease in RBC transfusions. Emergency surgery is not related to total transfusions, but it increased the intraoperative transfusion, there appears to be a need to apply an accurate transfusion guideline.

RBC transfusions for this study were conducted according to a transfusion guideline. Clinical indexes such as postoperative complications, ventilator support time, intensive care unit, and hospitalization reduced in the no-transfusion group. But there were no differences in mortality and major complications. Hematocrit also revived quickly after surgery leading around 35% hematocrit on their first outpatient department visit. This inversely proves that the standard for RBC transfusions used in this study is clinically appropriate (Tables 2, 3).

This study is a retrospectively and was not randomized, so it can have many limitations. There are no differences in seriousness of diseases such as 3 vessel disease or left main disease, or in frequency of emergency surgeries between the two groups, but disturbing variables such as difficulty level of surgery were not revised. However, the results of this study can provide data to minimize transfusions during OPCAB.

CONCLUSION

In this study, we performed the transfusion according to our transfusion guideline and over 40% cases could conduct the OPCAB without transfusion. There was no difference in major clinical results between transfusion and non-transfusion group. In addition, when used together with accurate understanding of patient factors, and reduced graft harvesting and operation time, it is expected to increase the proportion of patients that do not undergo transfusions.

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