

## The impact of blood use on patients undergoing coronary artery bypass surgery: a prospective study

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**SUMMARY:** The impact of blood use on patients undergoing coronary artery bypass surgery: a prospective study.

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**Objectives.** This survey aimed at assessing the incidence of blood use and the impact of cardiopulmonary bypass (CBP), sex, age, number of grafts, combined cardiac interventions, and hematocrit level in patients who undergo coronary artery bypass graft (CABG) surgery.

**Patients and Methods.** A prospective study included patients in the department of cardiac surgery at the American Hospital, in Tirana, Albania. We studied 164 consecutive patients who underwent CABG surgery over a 2-year period (2011-2013).

**Results.** We analyzed 164 patients: 138 men and 26 women. The average age was 61.8 years (range, 34–82 years). Of these, 116 patients (101 men/15 women) and 48 patients (37 men/11 women) were operated on-pump and off-pump, respectively. Packed red blood cells (PRBC) were administered to 79.87% of patients (131/164). In total, 334 units were transfused. The average number of PRBC units per patient was  $2.03 \pm 1.5$  (range, 0-8 units). Blood transfusion was administered to 87.06% and 62.5% of on-pump and off-pump patients, respectively. On-pump and off-pump patients received 2.4 and 1 unit of

PRBC, respectively ( $p < 0.001$ ). Female and male patients received 2.2 and 2 units, respectively ( $p = 0.1$ ). Patients aged  $\geq 62.5$  years received 2.3 units on average versus the average of 1.7 units received by patients aged  $< 62.5$  years ( $p < 0.001$ ). Interventions with 4-6 grafts (79/164) received an average 2.5 units, while those with 1-3 grafts (85/164) received 1.5 units ( $p < 0.001$ ). Patients requiring other cardiac surgical interventions (35/164) received an average of 2.6 units, while those without other cardiac surgical interventions (129/164) received an average of 1.8 units ( $p < 0.001$ ). Patients with preoperative hematocrit  $< 35\%$  received an average 1.2 units of PRBC intraoperatively, and 2.8 units throughout the hospital stay, while patients with preoperative hematocrit  $\geq 35\%$  received an average of 0.75 units intraoperatively ( $p < 0.001$ ) and 1.9 units throughout the hospital stay ( $p < 0.001$ ).

**Conclusion.** Blood transfusion was required for 79.87% of patients. Five variables were important factors in the use of blood in patients undergoing CABG: using CBP, a higher number of grafts, age  $\geq 62.5$  years, combined heart interventions and preoperative hematocrit  $< 35\%$ . Female patients required more PRBC than male patients, although it was not statistically significant. Knowledge of these risk factors enables better prediction of the probability of patients who might require more blood, better distribution of blood in CABG procedures, use by the blood bank, and evaluation of cost-effectiveness in the use of blood products.

KEY WORDS: Blood transfusion - Cardiac surgery - Graft.

### Introduction

Blood component transfusion is an important part of coronary artery bypass graft (CABG) surgery (1). Transfusion rates in cardiac surgery remain high despite major advances in preoperative blood conservation, and the transfusion practices for CABG surgery at different institu-

tions continue to vary significantly (2-7). The mean number of packed red blood cells (PRBC) transfused in CABG surgery ranges from 0 to 6.3 units per patient, and the frequency of transfusion ranges from 16% to 100% (1).

Not all patients are at the same risk for transfusion requirement. Some patient variables can be used to predict the risk for per operative transfusion (8). Although often lifesaving, blood transfusions are associated with significant risk to the patient and escalating cost to the blood bank system and hospital (9). The risks associated with the use of allogeneic blood product transfusion include ABO/Rh incompatibility, sepsis, febrile reactions, immunosuppression, and virus transmission (10, 13). Transmission of hepatitis B and C and HIV by transfusion occurs in 1 in 300.000 cases and non-fatal but serious transfusion errors occur in 1 in 16.000 transfusions (10).

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Blood transfusions have been linked to increased morbidity and mortality (11). Blood transfusion during or after CABG surgery was also associated with increased length of stay in the intensive care unit (ICU) and hospital (12).

This prospective study aimed at identifying the use of PRBC, the impact on surgery involving a cardiopulmonary bypass pump (CBP), demographic, number of grafts, patients requiring other cardiac surgical interventions and hematocrit (Hct) in patients who underwent CABG surgery at our cardiac surgery department over a 2-year period (from February 2011 to February 2013).

## Patients and methods

This study included all consecutive patients undergoing primary coronary artery surgery at our institution over a period of 2 years spanning February 2011 to February 2013. Until a few years ago, almost all CABG surgeries were performed with the use of CBP. In the last few years, there was a resurgence of interest in performing coronary artery surgery, popularly referred to as “beating heart surgery” without CBP. This study involved 164 patients (138 men and 26 women) who underwent CABG surgery that involved one of 2 methods: on-pump and off-pump. The surgery was either isolated (129/164 cases) or combined with other cardiac surgery (35/164 cases) over the study period at the department of cardiac surgery at American Hospital, Tirana, Albania. Of the 164 patients, 116 (101 men/15 women) underwent CABG surgery with CBP (on-pump) and 48 (37 men/11 women) underwent CABG surgery without CBP (off-pump). The average age of the patients was 61.8 years (range, 34–82 years).

Patients were reviewed for their preoperative demographic, clinical, and laboratory variables. One surgical team operated on all of the patients in this study. All cardiac medications were continued until the day of surgery, except antiplatelet drugs, which were stopped 5 days prior to surgery in elective patients. Anesthetic technique was standardized in all patients. Patients were premedicated with 7.5 mg midazolam orally the night before surgery and 10 mg morphine intramuscularly 30 minutes before they were sent to the operation theatre. Anesthesia was induced with 0.05–0.1 mg/kg midazolam, 5–10 g/kg fentanyl, and 0.1 mg/kg pancuronium to facilitate endotracheal intubation and mechanical ventilation. Fentanyl and pancuronium supplements were administered as required. All patients were monitored through a central arterial and venous catheter. After intubation, patients remained on mechanical ventilation with intermittent positive pressure with a tidal volume of 8–10 mL/kg, positive pressure at the end of expiration of 5–8 cm H<sub>2</sub>O, and fraction of inspired oxygen of 0.6–1 to maintain arterial oxygen saturation > 95%. Nitroglycerine and sodium nitroprusside were used in the intravascular route as vasodilators, dobutamine and dopamine as inotropics, and noradrenaline and adrenaline as vasopressors. All surgical procedures, i.e., on-pump and off-pump, were performed via median sternotomy.

PRBC are transfused according to the needs of each patient. At our clinic, blood transfusion was used to maintain Hct > 25% and hemoglobin (Hb) > 8.5 g/dL during cardiac surgery.

Activated clotting time (ACT) is measured before surgery. All on-pump patients required 2 g Transamin (tranexamic acid) as an antifibrinolytic agent at the start of anesthesia. For on-pump patients, anticoagulation was achieved with an initial dose of 300 U/kg heparin injected into the central venous system with ACT > 400 se-

conds (3–5 minutes after administration of heparin). For off-pump patients, 100–200 U/kg heparin was used to maintain ACT > 300–350 seconds. In both groups, we used heparin to maintain the ACT above the target sign during surgery. At the end of the bypass procedure, the effect of heparin was reversed with protamine chloride at a ratio of 1:1 (1:1.2). We also used an additional dose of protamine to return the ACT to the preoperative values (120–140 seconds). Platelet count and homeostasis test were carried out after heparin antagonization. Mean arterial blood pressure was maintained at 50–70 mmHg.

We used autologous vein grafts (saphenous vein) or artery grafts (mammary, internal thoracic, and radial artery). On average, on-pump surgery lasted 2.5–4 hours and was easily accomplished with systemic hypothermia (32–34°C); off-pump surgery lasted 2–3 hours and was achieved with normothermia. In on-pump and off-pump surgery, a cell salvaging unit (BRAT 2 Autologous Blood Recovery System; COBE Cardiovascular, Inc., Arvada, CO, USA) was used occasionally to retransfuse the patient at the end of the procedure. Patients were transferred to the ICU, intubated, and mechanically ventilated until they were ready to be woken. Monitoring; sedation; and analgesia, inotropic, and vasoactive administration were managed according to ICU protocol.

### Statistical methods

This prospective study involved consecutive patients who underwent elective or emergency CABG surgery. The data are summarized as the mean and 95% confidence interval. We considered  $p < 0.05$  statistically significant. The differences between the data for male and female patients were assessed by comparing the average  $t$ -test and analysis of variance. The impact of blood transfusion on CBP use, preoperative Hct < 35%, sex, and age  $\geq 62.5$  years (median values used as dividing points) was examined using a logistic regression model.

## Results

This prospective observational study involved 164 patients presenting for primary CABG surgery. The average age of the patients was 61.8 years (range, 34–82 years). Figure 1 illustrates the patient distribution according to age.

During surgery, 79.87% of patients (131/164) received PRBC. In total, 334 units of PRBC were used. The average amount of PRBC transfused to each patient was 2.03 units (range, 0–8 units). PRBC were not transfused in 20.12% (33/164) of patients, whereas 101 of 131 patients (77.09%) to whom PRBC were transfused received only 1–3 units of PRBC. The overall distribution of PRBC units to patients is depicted in Figure 2.

### 1. Impact of CBP on blood transfusion

On-pump patients received more PRBC than off-pump patients did. Specifically, 87.06% (101/116) of on-pump patients received PRBC as compared to 62.5% (30/48) of off-pump patients. On average, on-pump patients received 2.43 units versus the 1.06 units of PRBC received by off-pump patients ( $t = 8.2$ ,  $p < 0.001$ ). The units of PRBC received by on-pump and off-pump patients are shown in Figure 3.

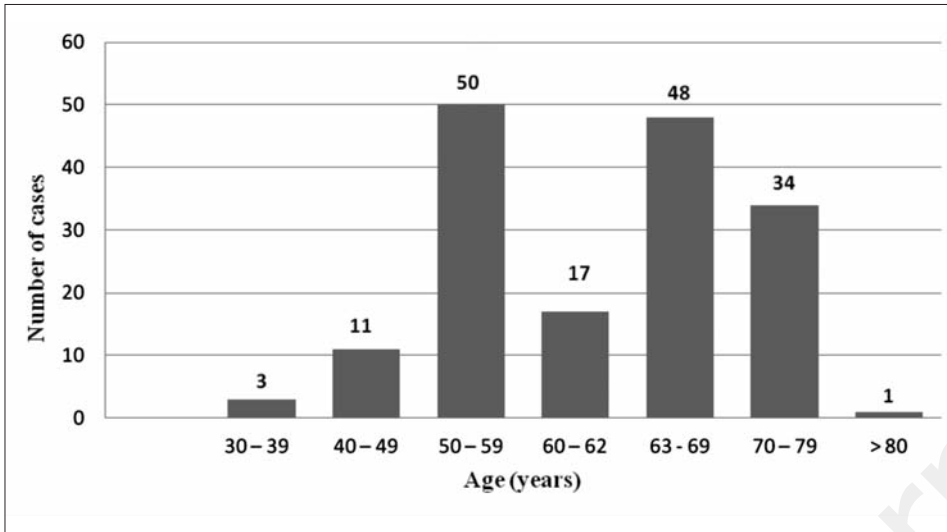


Fig. 1 - Number of patients according to age.

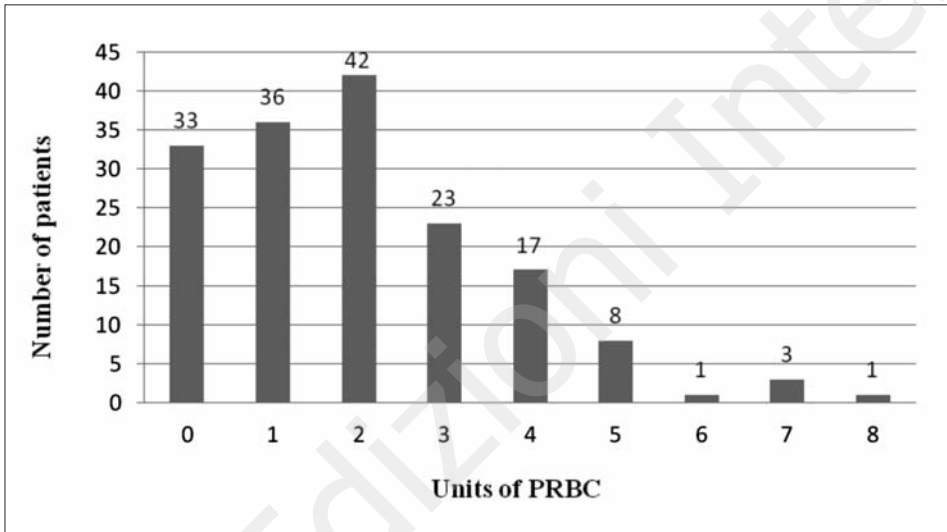


Fig. 2 - Distribution of PRBC units to all patients.

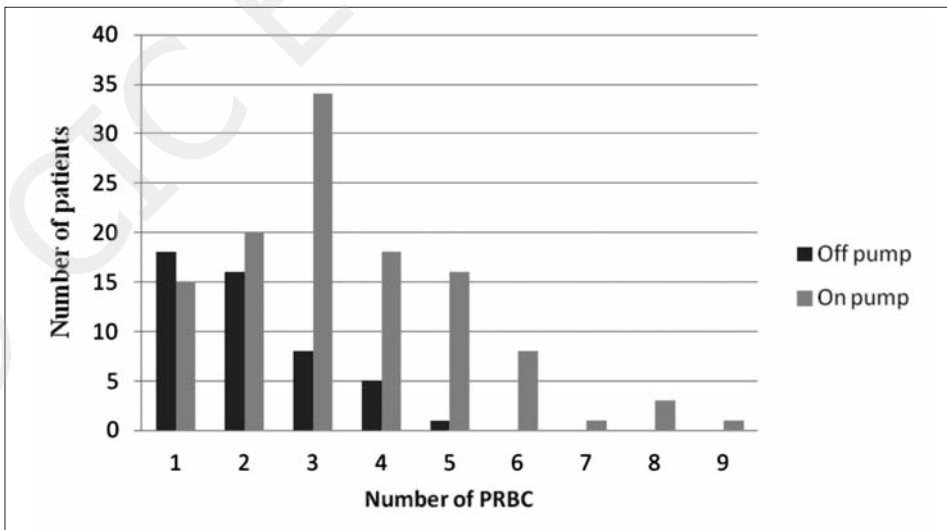


Fig. 3 - Distribution of PRBC units to on-pump and off-pump patients.

## 2. Impact of sex in blood transfusion

Overall, 80.7% (21/26) of women and 79.7% (110/138) of men received PRBC. Female patients received 2.2 units of PRBC during surgery, whereas male patients received 2 units of PRBC ( $t = 1.6$ ,  $p = 0.1$ ). Female patients received more PRBC than male patients did, although it was not statistically significant. The impact of sex on blood transfusion is presented in Table 1.

## 3. Influence of age on blood transfusion

Patients aged  $\geq 62.5$  years were transfused more often than younger patients were. In patients aged  $\geq 62.5$  years, 50.6% (83/164) received an average 2.3 units of PRBC, while 49.39% of patients (81/164) aged  $< 62.5$  years received an average 1.7 units of PRBC ( $t = 4.68$ ,  $p < 0.001$ ). The influence of age on blood transfusion is presented in Table 2.

## 4. Impact of graft number on blood transfusion

A larger number of grafts is associated with increased use of PRBC, therefore surgery involving 4-6 grafts in 48.17% (79/164) of patients required 2.5 units of PRBC, and 1.5 units of PRBC were required in the surgeries of 51.82% of patients (85/164) that required 1-3 grafts ( $t = 7.4$ ,  $p < 0.001$ ). The impact of the number of grafts on blood transfusion is presented in Table 3.

## 5. Impact of combined cardiac surgical interventions

Other cardiac surgical interventions were associated with

greater use of blood transfusion than isolated surgery (without other cardiac surgical intervention). Patients who underwent other cardiac surgical interventions (35/164, 21.34%) received an average 2.6 units of PRBC, while patients who underwent no other cardiac surgical intervention (129/164, 78.65%) received an average 1.8 units of PRBC ( $t = 4.7$ ,  $p < 0.001$ ). The impact of other cardiac surgical interventions is presented in Table 4.

## 6. Impact of preoperative Hct on blood transfusion

Low preoperative Hct is associated with greater use of blood transfusion intraoperatively and throughout the hospital stay. Of the patients studied, 13.41% (22/164) had preoperative Hct  $< 35\%$  and 86.58% (142/164) had preoperative Hct  $\geq 35\%$ .

### a. Impact of preoperative Hct on blood transfusion during surgery

Intraoperative PRBC was administered to 86.36% (19/22) of patients with preoperative Hct  $< 35\%$ . These patients received an average 1.2 units of PRBC. Intraoperative PRBC was administered to 60.68% (88/145) of patients with preoperative Hct  $\geq 35\%$ . These patients received an average 0.7 units of PRBC ( $t = 2.56$ ,  $p < 0.001$ ). The influence of preoperative Hct on intraoperative blood transfusion is shown in Table 5.

### b. Impact of preoperative Hct on blood transfusion throughout the hospital stay

Blood was transfused throughout the hospital stay for 86.36% (19/22) of patients with preoperative Hct  $< 35\%$ ;

TABLE 1 - IMPACT OF SEX ON BLOOD TRANSFUSION.

Sex	Number of patients	Transfused patients	Average number of PRBC units received	p-value
Female	26	21 (80.7%)	2.2	0.1
Male	138	110 (79.7%)	2	

TABLE 2 - INFLUENCE OF AGE ON BLOOD TRANSFUSION.

Age	Number of patients	Average number of PRBC units received	p-value
$\geq 62.5$ years	83	2.3	$< 0.001$
$< 62.5$ years	81	1.7	

TABLE 3 - IMPACT OF THE NUMBER OF GRAFTS ON BLOOD TRANSFUSION.

Number of grafts	Number of patients	Average number of PRBC units received	p-value
1-3	85	1.5	$< 0.001$
4-6	79	2.5	

TABLE 4 - IMPACT OF COMBINED CARDIAC SURGICAL INTERVENTIONS ON BLOOD TRANSFUSION.

Variables	Number of patients	Average number of PRBC units received	p-value
Isolated CABG	129	1.8	$< 0.001$
Combined CABG	35	2.6	

TABLE 5 - INFLUENCE OF PREOPERATIVE HCT ON INTRAOPERATIVE BLOOD TRANSFUSION.

Hct	Number of patients	Intraoperative blood transfusion	Average number of PRBC units received	p-value
<35%	22	19 (86.36%)	1.2	<0.001
≥35%	142	88 (61.97%)	0.7	

TABLE 6 - IMPACT OF PREOPERATIVE HCT ON BLOOD TRANSFUSION THROUGHOUT THE HOSPITAL STAY.

Hct	Number of patients	Transfused	Average number of PRBC units received	p-value
<35%	22	19 (86.36%)	2.8	<0.001
≥35%	142	111 (78.16%)	1.9	

an average of 2.8 units of PRBC were used. Blood was transfused for 78.16% of patients with preoperative Hct  $\geq 35\%$  during their stay in hospital, and an average 1.9 units of PRBC were used ( $t = 4.8$ ,  $p < 0.001$ ). The impact of preoperative Hct on blood transfusions throughout the hospital stay is presented in Table 6.

## Discussion

Bleeding and transfusion of blood and blood components are frequent surgical complications among patients undergoing CABG surgery with a CBP pump (13). The incidence of blood transfusion among patients undergoing coronary artery surgery has been reported to be between 27% and 92% (6).

The goal of our investigation was to examine the impact of 5 major variables (CBP, sex, age, number of grafts, associated cardiac surgeries) on blood use in patients undergoing CABG surgery at our institution over a period of 2 years. We found that on-pump (versus off-pump), female gender, age  $\geq 62.5$  years, a large number of grafts, associated heart disease, and preoperative Hct  $< 35\%$  were significant predictors of blood transfusion for patients undergoing coronary artery surgery; however, the findings for female patients as compared to male patients were not statistically significant. Preoperative Hct was one of the predictors of blood transfusion in previous reports (14-16). We found that it was the most significant predictor of blood transfusion. Use of a CBP pump was the second most significant predictor of blood transfusion.

The next significant predictor of transfusion in CABG surgery was sex. Female gender was identified as a risk factor for blood transfusion in patients undergoing CABG surgery. This has been noted in both on-pump and off-pump surgery (14, 16-18). Our results are in agreement with these previous reports.

In a Japanese study, Isomatsu *et al.* (19) studied 89 patients who underwent isolated CABG surgery over 2

years from 1997 to 1999 to determine preoperative predictors of the need for blood transfusions during CABG surgery. Sixty-six patients (74%) received transfusions during hospitalization. The independent predictors were emergency surgery, lower Hct, older age, and presence of peripheral vascular disease. The optimal cutoff for Hct and age was 39% and 64 years, respectively.

Karkouti *et al.* (14) studied patients undergoing elective primary CABG surgery prospectively. The transfusion rate was 29.4%. Predictors included preoperative Hb, weight, age, and sex.

Scott *et al.* (20) studied the impact of CBP, Hct, sex, age, and body weight on blood use in 1235 patients undergoing primary CABG over a period of 2 years under on-pump or off-pump technique. PRBC was received by 72.5% of on-pump patients as compared with 45.7% of off-pump patients. Fewer male (52.6%) than female patients (79.4%) received transfusion. Use of CBP, preoperative Hct  $< 35\%$ , female gender, increased age ( $\geq 65$  years), and decreased body weight ( $< 83$  kg) were significant predictors of transfusion. The strongest predictors of PRBC transfusion were preoperative Hct  $< 35\%$  and use of CBP.

Al-Shammari *et al.* (21) reviewed the medical records of 159 consecutive primary CABG patients retrospectively to determine the preoperative factors associated with intraoperative blood transfusion. Overall, 128 (80.5%) patients received blood product transfusion intraoperatively, of which 113 (70.5%) received PRBCs and the rest received fresh frozen plasma and platelets. Moreover, 23 patients (12.6%) received more than 2 units of PRBC intraoperatively. Altogether, 159 patients required 342 units of PRBCs at an average of 2.1 units per patient. The significant factors associated with intraoperative PRBC transfusion were age  $> 60$  years, female gender, preoperative Hb  $< 12$  g/dL, and construction of  $\geq 3$  coronary bypass grafts.

In a large series, Frankel *et al.* (22) compared 3646 off-pump CABG patients with a contemporaneous con-

trial group of 5197 on-pump CABG patients. Off-pump CABG surgery was associated with a reduced need for single- and multiple-unit postoperative blood transfusions as compared to on-pump CABG surgery. In addition, Nader *et al.* (23) compared on-pump and off-pump patients. They found that the off-pump group required fewer blood products than the on-pump group, which may have been accompanied by a concurrent decrease in the risk of blood-borne pathogen transmission, blood transfusion reactions, and the associated risk of nonautologous transfusion.

On the contrary, in a multicenter randomized study on 160 selected low-risk patients undergoing CABG surgery on-pump (80 patients) or off-pump (80 patients), Gerola *et al.* (24) did not find any statistical difference in blood component use between on-pump and off-pump patients; 43.7% of on-pump patients and 43% of off-pump patients received blood component transfusion. The number of blood units used in on-pump patients was  $2.9 \pm 1.8$  units per patient and  $2.2 \pm 1.3$  units per patient in off-pump patients.

The limitations of our study are the inclusion of scheduled and non-scheduled (urgent) patients; the latter has

an increased risk for blood transfusion. Likewise, patients who underwent CABG and cardiac catheterizing (coronarography procedure) in the same admission were at risk for transfusion. The number of female patients was relatively limited (26/164). We did not consider other variables such as the duration of surgery, and the surgeon and anesthesiologist.

In conclusion, we examined the impact of CBP, d, number of grafts, combined heart disease procedures, and preoperative Hct at our institution. We found that all 5 variables were significant predictors of blood use in patients undergoing CABG. Preoperative Hct  $\leq 35\%$  and use of a CBP pump were the strongest predictors of transfusion. Knowledge of these risk factors enables better prediction of the probability of patients requiring increased blood use, better distribution of blood in CABG procedures, use by the blood bank, and evaluation of cost-effectiveness in the use of blood products.

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