Article

Use of Cell Saver in Elective Coronary Bypass Surgery: What Do We Risk When Saving Blood?

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Use of Cell Saver in Elective Coronary Bypass Surgery: What Do We Risk When Saving Blood?

Adem Reyhancan *, Mürsel Büyükadalı, Ertuğrul Koçak, Orkut Güçlü, Serhat Hüseyin and Suat Canbaz

Department of Cardiovascular Surgery, Faculty of Medicine, Trakya University, Edirne, Türkiye

* Correspondence: areyhancan@gmail.com; Tel.: +90-539-745-4443

Abstract: Background/Objectives: Allogeneic transfusion is a commonly used method to replace blood and blood elements lost during cardiac surgery, but it also has quite undesirable effects. The use of Cell Saver is now almost routinely recommended. The aim of this study is to investigate the clinical and laboratory outcomes of the use of Cell Saver in elective CABG. **Methods**: Patients who had undergone elective CABG between January 2022 and October 2024 were retrospectively analyzed, and 344 patients were included in the study. Patients were divided into two groups: Cell Saver used (CS, n=110) and not used (NCS, n=234). The groups were compared in terms of pre- and postoperative clinical and laboratory outcomes. **Results**: The mean age of the cases included in the study was 63.65±9.05 years (340 patients, range 36-87). The mean amount of drainage in the first 6 hours postoperatively was 298.18±155.81 ml in the NCS group and 388.64±173.62 ml in the CS group (p<0.001). In the first 24 hours it was 703.22±320.39 ml in the NCS group and 827.73±344.69 ml in the CS group (p=0.001). Prolonged drainage was more frequent in the CS group (p=0.004) and the length of hospital stay was longer (p=0.014). The postoperative albumin level was lower in the CS group (p=0.003). **Conclusions**: Although the use of Cell Saver reduces the need for allogeneic transfusions, it leads to increased bleeding in the initial period, prolonged drainage and thus to a longer hospital stay. In elective procedures, blood management should be evaluated and optimized using all methods.

Keywords: cell saver; blood; drainage; albumin; coronary

1. Introduction

Coronary artery disease remains a major cause of morbidity and mortality in both developed and developing countries[1]. Coronary artery bypass grafting (CABG) is one of the most commonly performed procedures in the treatment of coronary artery disease. According to the Society of Thoracic Surgeons report, 65-74% of annual cardiac surgeries are isolated CABGs. Approximately 90% of these operations are performed with cardiopulmonary bypass (CPB)[2]. These procedures can result in significant blood loss due to CPB and the type of surgical techniques used[3]. This often necessitates perioperative and postoperative allogeneic blood transfusions. However, allogeneic blood transfusions are associated with several adverse outcomes, including immunomodulation, increased risk of infection, hemolytic reactions and higher healthcare costs[4–6]. Therefore, intraoperative blood management and autologous blood collection have become increasingly important in recent years[7].

The Cell Saver was developed to collect blood spilled during surgery, process it by centrifugation and filtration and return the red blood cell concentrated autologous blood to the patient. This method is a safe and effective means of reducing the need for allogeneic transfusions[8]. Nevertheless, the impact of the use of Cell Saver on postoperative laboratory parameters and clinical outcomes is a topic of ongoing debate.

The aim of this study is to investigate the impact of Cell Saver use on postoperative hematologic and biochemical parameters, transfusion requirements, and clinical outcomes in patients undergoing elective isolated CABG surgery to provide objective data for routine use in clinical practice.

2. Materials and Methods

2.1. The Population of the Study

All patients who underwent CABG at our center between January 2022 and October 2024 were retrospectively analyzed. Patients with previous cardiac surgery, a permanent pacemaker, chronic atrial fibrillation and known hereditary blood clotting disorders were excluded from the study. In our clinic, P2Y12 inhibitors are discontinued at least 5 days before surgery; factor Xa inhibitors are discontinued at least 72 hours before surgery. Patients who did not fulfill these criteria were also excluded from the study. The study included 344 patients who underwent elective isolated on-pump CABG via median sternotomy. The cases were analyzed in two groups: Patients who underwent surgery during the period when the Cell Saver device and disposable sets were not available at our center were referred to as the No Cell Saver group (NCS, n=244) in our study, and patients who had used a Cell Saver during surgery were referred to as the Cell Saver group (CS, n=110).

2.2. The Use of Cell Saver

All operations were performed via a median sternotomy. In both groups, after systemic heparinization for CPB, the blood in the surgical field was aspirated with a cardiac aspirator only. In the CS group, the cardiac aspirator was not used after completion of CPB and start of protamine infusion. After this phase, the remaining blood in the reservoir of the CPB circuit was transferred to the cell saver (The Sorin EXTRA® autotransfusion system (Livanova, London, UK)). In the NCS group, cardiotomy suction was continued until the protamine infusion had reached half the dose. The blood remaining in the reservoir was delivered to the patient via the aortic cannula until the protamine dose was halved, paying attention to systemic arterial pressure and central venous pressure. The blood collected in the Cell Saver Reservoir was processed and reinfused before the patient left the operating theater.

2.3. Data Collection

Demographic data, preoperative risk evaluations (EuroSCORE II), comorbidities, body surface area (BSA) calculations, ejection fraction and the largest measured left atrial diameter of the patients were retrospectively analyzed. The number of grafted vessels, CPB and aortic cross clamping (ACC) time were recorded. Activated clotting time (ACT) values before systemic heparinization, after neutralization with protamine and during ICU admission were recorded. Drainage volumes at the end of the first 6 and 24 hours after surgery were assessed using the intensive care unit (ICU) follow-up charts.

Complete blood count (CBC), coagulation and other biochemical parameters were determined and recorded for each patient on preoperative day 1, day 1 and day 4 after surgery. The number of red blood cell (RBC) transfusions received by the patients during their hospitalization was recorded. Transfusions were performed in cases where the hemoglobin level was <8 gr/dL or <9 gr/dL with anemia symptoms such as hypoxia, hypotension, and tachycardia. Postoperative complications such as pneumonia, prolonged drainage, new-onset atrial fibrillation (NOAF), re-exploration, reintubation, acute kidney failure (AKF), cerebrovascular accident (CVA) and mortality were recorded during the 30-day postoperative period. Prolonged drainage was defined as the inability to remove the chest tube for more than 4 days due to the amount of drainage. The two groups were compared with regard to these outcomes.

2.4. Statistical Analysis

Statistical analysis was performed using SPSS software for Windows version 23.0 (IBM Corp., Armonk, NY, USA). Descriptive data are presented as mean ± standard deviation (SD) or as number

and frequency. The distribution of variables was measured using the Kolmogorov-Smirnov test. The chi-square test was used to analyze independent qualitative data, and Fisher's exact test was used when the conditions of the chi-square test were not met. Student's t-test was used for independent quantitative data when variances were homogeneously distributed. The Mann-Whitney U-test was used when the variances were not homogeneously distributed. A p-value of <0.05 was considered to indicate statistical significance.

3. Results

The mean age of the cases included in the study was 63.65 ± 9.05 years (340 patients, range 36-87). There were no significant differences between the groups in terms of demographic data and preoperative risk assessments. The proportion of male patients was higher in the CS group (80.9%) than in the NCS group, but no statistically significant difference was found (p<0.083). The mean ejection fraction and left atrial diameter were respectively 54.2 ± 7.4% and 35.9 ± 4.7 mm in the CS group, while they were 53.4 ± 7.8% and 36.7 ± 4.6 mm in the NCS group (p>0.05). When the two groups were compared for the mean number of vessels grafted, no significant difference was found (CS, 3.3 ± 0.8; NCS, 3.2 ± 0.9; p>0.05). CPB and ACC times were similar between the two groups. The demographic data and the comparison of preoperative and intraoperative findings are summarized in Table 1.

Table 1. Preoperative assessment and surgical data.

	NCS (n= 234)	CS (n= 110)	P
Age (year)	63.7 ± 8.9	63.6 ± 9.3	0.966
BSA (m2)	1.89 ± 0.17	1.89 ± 0.19	0.830
EuroScore II	1.48 ± 0.95	1.46 ± 0.92	0.849
Biological Sex			0.083
Female	65 (27.8%)	21 (19.1%)	
Male	169 (72.2%)	89 (80.9%)	
Comorbidities			
Diabetes Mellitus	112 (47.9%)	52 (47.3%)	0.919
Hypertension	168 (71.8%)	80 (72.7%)	0.857
COPD	14 (6%)	8 (7.3%)	0.826
CVA	18 (7.7%)	9 (8.2%)	>0.99
GFR <50 mL/min	43 (18.4%)	16 (14.5%)	0.468
Ejection Fraction (%)	54.2 ± 7.4	53.4 ± 7.8	0.355
LA diameter (mm)	35.9 ± 4.7	36.7 ± 4.6	0.201
Number of grafted vessels	3.2 ± 0.9	3.3 ± 0.8	0.431
CPB time (min)	106.16 ± 30.36	102.88 ± 24.74	0.241
ACC time (min)	54.81 ± 17.38	52.80 ± 14.70	0.294

ACC, *aortic cross clamp*; BSA, *body surface area*; CPB, *cardiopulmonary bypass*; LA, *left atrium*

In the CS group, the mean amount of blood reinfused into the patients with Cell Saver was 568.25 ± 197.94 (range 160 to 1050 ml). The mean amount of drainage at the end of the first 6 hours after surgery was 298.18 ± 155.81 ml in the NCS group and 388.64 ± 173.62 ml in the CS group. At the end of the first 24 hours, it was 703.22 ± 320.39 ml in the NCS group and 827.73 ± 344.69 ml in the CS group. Both at the end of the first 6 hours and in the first 24 hours after surgery, there was statistically significantly more bleeding in the patients in the CS group (p< 0.001 for the first 6 hours and p= 0.001 for the first 24 hours). Considering the possible incorrect evaluations arising from the differences in BSA of the patients, the drainage amounts were compared again by proportioning them to BSA, and similarly, the amount of bleeding was found to be higher in the CS group patients. On the other hand, it was found that the mean amount of RBC transfusions in the NCS group was 3.82 ± 2.37 bags, while

in the CS group it was 2.95 ± 2.05 bags (p= 0.001). Re-exploration due to bleeding was required in 6 (2.6%) patients in the NCS group and 7 (6.4%) patients in the CS group. Although this occurred more frequently in the CS group in percentage terms, no statistically significant difference was found (p>0.05).

The mean extubation time was 6.14 ± 4.08 hours in the NCS group and 6.29 ± 3.87 hours in the CS group (p>0.05). When comparing the need for reintubation, no significant difference was found between the two groups. Patients in the NCS group stayed in the ICU for 2.4 ± 2.6 days, while patients in the CS group stayed for 2.2 ± 0.7 days (p>0.05).

Prolonged drainage was observed in 35 (15.2%) patients in the NCS group and in 31 (28.2%) patients in the CS group. Prolonged drainage was statistically significantly more frequent in the CS group (p=0.004). Patients in the NCS group were discharged after 8.5 ± 4.5 days, while this period was 9.9 ± 5.5 days in the CS group. Patients in the CS group had a statistically significantly longer hospital stay (p=0.014).

No significant difference was found between the two groups in terms of pneumonia, NOAF, AKF, CVA, rehospitalization and mortality in the 30-day postoperative period.

The comparison of clinical outcomes in the postoperative period is shown in Table 2.

Table 2. Clinical results in the postoperative phase.

	NCS (n= 234)	CS (n= 110)	P
Cell Saver Volume (mL)	0	568.25 ± 197.94	**< 0.001**
Drainage in 6h (mL)	298.18 ± 155.81	388.64 ± 173.62	**<0.001**
Drainage Index (mL/m2)	*159.42 ± 85.13*	*207.23 ± 95.78*	***<0.001***
Drainage in 24h (mL)	703.22 ± 320.39	827.73 ± 344.69	**0.001**
Drainage Index(mL/m2)	*374.26 ± 172.89*	*440.54 ± 192.08*	***0.002***
RBC transfusion (bag)	3.82 ± 2.37	2.95 ± 2.05	**0.001**
Extubation Time (h)	6.14 ± 4.08	6.29 ± 3.87	0.750
Reintubation	8 (3.5%)	6 (5.5%)	0.392
Reexploration	6 (2.6%)	7 (6.4%)	0.126
Prolonged Drainage	35 (15.2%)	31 (28.2%)	**0.004**
Pneumonia	11 (4.7%)	8 (7.3%)	0.340
NOAF	94 (40.2%)	47 (42.7%)	0.653
AKF	9 (3.9%)	3 (2.8%)	0.759
CVA	3 (1.3%)	0 (0%)	0.554
ICU Stay (day)	2.4 ± 2.6	2.2 ± 0.7	0.470
Hospital Stay (day)	8.5 ± 4.5	9.9 ± 5.5	**0.014**
Rehospitalization	15 (6.6%)	3 (2.7%)	0.142
Mortality	7 (3%)	0 (0)	0.102

AKF, *acute kidney failure*; BSA, *body surface area*; CVA, *cerebrovascular accident*; ICU, *intensive care unit*; NOAF, *new-onset atrial fibrillation*; RBC, *red blood cell*

ACT levels before systemic heparinization, after protamine neutralization and on admission to the ICU were compared between groups. The time between the last two ACT values corresponds to the time at which the processed waste blood was transfused to the patients in the CS group. In the CS group, the mean ACT was 124.76 ± 15.28 seconds before heparinization, 118.92 ± 12.53 seconds after protamine neutralization and 122.46 ± 13.53 seconds after transfusion of the processed blood. In the NCS group, the mean ACT was 126.01 ± 17.84 seconds before heparinization, 116.79 ± 12.81 seconds after protaminization and 117.25 ± 11.99 seconds on admission to the ICU. A statistically significant increase in ACT was observed after the processed blood transfusion in the CS group (p< 0.001).

A mean albumin level of 4.19 ± 0.43 in the NCS group and 4.14 ± 0.45 gr/dl in the CS group was found in the blood samples taken before the operation (p> 0.05). On the first postoperative day it was 3.51 ± 0.28 in the NCS group and 3.41 ± 0.32 gr/dl in the CS group; on the fourth postoperative day it was 3.29 ± 0.30 in the NCS group and 3.19 ± 0.29 gr/dl in the CS group. On the first and fourth postoperative day, the albumin level was statistically lower in the CS group (p= 0.003).

Mean hemoglobin and hematocrit levels were higher in the CS group before surgery than in the NCS group (p= 0.039 for hemoglobin; p= 0.057 for hematocrit). On the first postoperative day, there was a more significant statistical difference in the mean hemoglobin and hematocrit values of the patients in the CS group (p<0.001 for both). On the fourth postoperative day, no significant difference was found between the two groups in terms of hemoglobin and hematocrit (p= 0.316 for hemoglobin; p= 0.558 for hematocrit).

While the platelet count was similar between the two groups in the preoperative CBC (p>0.05), on the first postoperative day it was significantly lower in the CS group (p= 0.030). On the fourth postoperative day, no statistically significant difference was found between the two groups.

In the blood samples taken before the operation and on the first and fourth postoperative day, no significant difference was found between the groups in terms of CRP and INR values.

The comparison of the two groups in terms of blood test results is summarized in Table 3.

Table 3. Comparison of pre- and postoperative blood test results.

	NCS (n= 234)	CS (n= 110)	P
ACT (sec)			
Preoperative	126.01 ± 17.84	124.76 ± 15.28	0.529
Post-protamine	116.79 ± 12.81	118.92 ± 12.53	0.149
Admission to the ICU	117.25 ± 11.99	122.46 ± 13.53	**<0.001**
CRP (mg/L)			
Preoperative	16.21 ± 23.87	17.65 ± 26.96	0.616
Postoperative 1st day	75.42 ± 30.88	77.70 ± 39.43	0.561
Postoperative 4th day	92.38 ± 43.02	96.18 ± 48.93	0.467
Albumin (g/dL)			
Preoperative	4.19 ± 0.43	4.14 ± 0.45	0.289
Postoperative 1st day	3.51 ± 0.28	3.41 ± 0.32	**0.003**
Postoperative 4th day	3.29 ± 0.30	3.19 ± 0.29	**0.003**
Hemoglobin (g/dL)			
Preoperative	13.12 ± 1.78	13.54 ± 1.73	**0.039**
Postoperative 1st day	9.54 ± 0.69	9.91 ± 0.87	**<0.001**
Postoperative 4th day	10.36 ± 0.99	10.48 ± 0.99	0.316
Hematocrit (%)			
Preoperative	38.75 ± 4.99	39.83 ± 4.69	0.057
Postoperative 1st day	27.76 ± 2.32	28.96 ± 2.59	**<0.001**
Postoperative 4th day	30.82 ± 3.06	31.03 ± 2.97	0.558
Platelet (10^3 μL)			
Preoperative	279.74 ± 83.04	270.27 ± 76.86	0.313
Postoperative 1st day	218.66 ± 64.39	203.45 ± 51.29	**0.030**
Postoperative 4th day	218.59 ± 71.29	207.51 ± 55.21	0.253
INR			
Preoperative	1.016 ± 0.076	1.009 ± 0.078	0.453
Postoperative 1st day	1.099 ± 0.072	1.099 ± 0.080	0.954
Postoperative 4th day	1.049 ± 0.083	1.052 ± 0.111	0.808

ACT, *activated clotting time*; CRP, *C-reactive protein*, INR, *international normalized ratio*

4. Discussion

Allogeneic blood transfusions are a common method to maintain tissue oxygenation and hemostasis at an adequate level, as bleeding is relatively common in cardiac surgery. With the increasing number of studies over the last century and the discovery of the adverse effects of transfusion, new methods have been developed to minimize allogeneic blood transfusion in today's surgical practice. The use of cell savers is one of the most commonly used methods in this context. In our study, we concluded that the use of Cell Saver in elective CABG patients reduces the need for blood transfusion in the postoperative period, but delays clotting in the early period, resulting in more bleeding, prolonged drainage and a longer hospital stay.

In a randomized controlled study by Scrascia et al [9], which is similar to our practice, the blood remaining in the CPB reservoir was processed with Cell Saver and returned to a group of patients. In this group of patients, more bleeding was observed in the postoperative period. This was found to be related to increased fibrinolytic activity after the blood processed with the Cell Saver system was returned. In another randomized controlled trial, it was reported that the use of Cell Saver delayed clot formation and reduced the firmness of the clot, resulting in an increase in bleeding in the initial period.[10] Similarly, many studies have concluded that the use of Cell Saver in the initial phase increases bleeding. [11,12] In a prospective observational study, patients operated with the on-pump, off-pump + Cell Saver and off-pump methods were compared and it was found that the use of Cell Saver induced fibrinolysis as much as CPB. [13] In addition, there are also studies indicating that the use of Cell Saver is not associated with bleeding and actually reduces it. [14–16] In our study, the amount of bleeding was significantly higher in the CS group after the first 6 hours and at the end of 24 hours. A significant difference was observed between ACT times after protamine and at the time of ICU admission in the CS group. Although there are studies suggesting that there is no significant amount of residual heparin in the filtered blood of Cell Saver, it was observed in our study that ACT increased after transfusion. [17]

Another finding that we observed in our study as a reason for the increased bleeding in the CS group was the decrease in platelet count. On the first day after surgery, the platelet count was lower in the CS group than in the NCS group. Similarly, in the study by Campbell et al [10], it was observed that the platelet count in the postoperative period was lower in the cases where Cell Saver was used. In another study, more bleeding and lower platelet counts were observed at the end of the first 6 and 24 hours in cases where Cell Saver was used. [12] Processing the blood remaining in the CPB reservoir with Cell Saver and transfusing it to the patient also leads to a washout and excretion of platelets in the blood. [18]

In the CS group, although the amount of bleeding in the first 24 hours after surgery and the frequency of prolonged drainage in the following days were higher, the hemoglobin level in the early phase was higher and the need for allogeneic transfusions was lower. In our study, the hemoglobin level was significantly higher in patients in the CS group in the preoperative phase (p=0.039). However, on the first postoperative day, the statistical difference became more significant (p<0.001). This difference in hemoglobin levels between the two groups was no longer observed on the fourth postoperative day. Similar to our study, Al-Mandhari et al [11], reported that bleeding was higher in the cases where cell saver was used, but hemoglobin levels were higher in the early phase. In addition, fewer blood transfusions were required in the cases where Cell Saver was used, despite the high bleeding rate. Damgaard et al [15], found that hemoglobin levels were higher in the cases where Cell Saver was used, although bleeding and blood product requirements were similar. Reyes et al [12], reported that the bleeding rate was higher in the low-risk cases when Cell Saver was used, but there was no difference between the groups in terms of hemoglobin levels and blood consumption. When these three parameters are taken into account, the exact effect of using Cell Saver is controversial.

Cell Saver prepares an RBC-rich suspension by washing the blood from the surgical field and the CPB reservoir with saline. Pillay et al [19], showed that the amount of albumin in pump blood washed with saline was significantly reduced. In our study, the amount of albumin in the blood

samples taken on the first and fourth postoperative day was significantly lower in the CS group than in the NCS group. Hypoalbuminemia in the postoperative period was associated with increased bleeding in the initial period and prolonged hospital stay. [20] In the CS group, we observed both prolonged drainage and prolonged hospitalization. We think that increased bleeding and hypoalbuminemia in the initial phase led to prolonged drainage and thus prolonged hospitalization.

There are studies indicating that blood transfusions are a risk factor for NOAF regardless of their quantity, while there are also studies indicating that they are not a risk factor for NOAF. [21–23] Koçyiğit et al [24], reported that more blood transfusions were performed in cases with NOAF after CABG. It was also found that less NOAF was observed in cases in which cell saver was used than in the cases in which it was not used. There are also studies linking perioperative anemia and allogeneic blood transfusions to an increased incidence of ACF and CVA. [25,26] In our study, no significant difference was found when the CS and NCS groups were compared in terms of the incidence of ACF, CVA and NOAF in the postoperative period.

Limitations of This Study

Due to the retrospective design of this study, there is a risk of selection bias in patient selection and data collection. No propensity score matching was applied to adjust for potential confounding variables between groups, which should be considered a factor that may limit internal validity in between-group comparisons. Although the extent of bleeding in the postoperative period was analyzed, advanced coagulation analyzes such as thromboelastography (TEG) or rotational thromboelastometry (ROTEM) were not used for a detailed assessment of hemostatic function, but only routine laboratory parameters (PT, aPTT, INR, fibrinogen, platelet count, etc.). These methodological limitations require a cautious interpretation of the results obtained and limit the possibility to draw causal conclusions.

5. Conclusions

In conclusion, we believe that although the use of Cell Saver in elective CABG procedures results in fewer allogeneic transfusions, it increases bleeding in the postoperative period and consequently leads to prolonged drainage and a longer hospital stay. In elective CABG procedures, where relatively low intraoperative bleeding is expected compared to other cardiac surgical procedures, the most appropriate method for the patient should be considered along with other blood management techniques to reduce the need for transfusion. Blood management is a sensitive issue that should be evaluated in its entirety before, during and after surgery.

Abbreviations

The following abbreviations are used in this manuscript:

ACC Aortic cross clamping
AKF Acute kidney failure
ACT Activated clotting time
CABG Coronary artery bypass grafting
COPD Chronic obstructive pulmonary disease
CPB Cardiopulmonary bypass
CRP C-reactive protein
CVA Cerebrovascular accident
GFR Glomerular filtration rate
INR International normalized ratio
LA Left atrium
NOAF New-onset atrial fibrillation
RBC Red blood cell

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