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Blood Loss and Intraoperative Salvage Procedure in Patients Underwent Coronary Artery Bypass Reoperative Surgery

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Abstract

Preoperative patients` characteristics can predict the need for perioperative blood component transfusion in cardiac operations. Currently, a large number of patients are on antiplatelet therapy. A group of these patients require reoperative surgery (redo) after coronary artery bypass grafting (CABG). We aimed to compare blood loss in patients having CABG with patients undergoing reoperative CABG surgery. Fifty-four patients (16% female, 84% male; ages 60.5 ± 6 *vs.* 66.2 ± 7 years) were divided in: Group 1–CABG, and Group 2–redo CABG. Blood samples were collected: 24h prior, 6h and 24h after the operation. We measured hematological parameters and total amount of blood products substituted. Preoperative clopidogrel and aspirin therapy were not statistically significant (p=0.094), while platelet count (p=0.002) was significantly lower in Group 2. Although we have found some differences in the blood drained (868.5 ± 587 *vs.* 1088 ± 819 mL) it was not statistically relevant (p=0. 28). Allogenic erythrocytes substituted intraoperatively were not statistically different (p=0.61), while autologous blood salvage procedure was weakly significant (p=0.05). Platelets transfused (p=0.88), fresh frozen plasma (p=0.68), and packed red blood cells transfused postoperatively (p=0.32) have not reached statistical significance. Length of stay in intensive care unit (ICU) was not influenced by used blood components transfusion, either allogenic or autologous. We have found positive correlation between blood loss and ICU stay (r=0.49, p=0.021). Monitoring of these parameters offers an important addition to the preoperative risk assessment.

Keywords: Blood loss; Cell salvage procedure; Coronary artery bypass reoperative surgery

Introduction

Despite advances in surgical techniques, microvascular bleeding is a major problem that occurs after open heart surgery [1]. A large number of patients are currently on antiplatelet inhibition using aspirin or clopidogrel. A group of these patients requires reoperative surgery (redo) after coronary artery bypass grafting (CABG). During the operation they received unfractioned heparin [2]. Due to the re-exploration of chest these patients are at higher risk of perioperative bleeding [3] and require consequential transfusion of blood products. The need for allogeneic red blood cell (RBC) transfusion was reported intraoperatively and in the early postoperative course at surgical Intensive Care Units (ICUs) [4-7]. Unfortunately, allogenic blood transfusion has been associated with increased risk of infectious and non-infectious complications. Donor's erythrocytes should be compatible and sophisticated techniques are necessary to prevent allergic reactions to blood products [8].

Intraoperative blood salvage is the procedure by which the blood from surgical field is collected, washed, and filtered to produce autologous blood for transfusion back to the patient's circulation [8]. Commonly known as autologous blood transfusion or cell salvage process, it has been used for many years and evolved since 1960s [8]. That way the patient receives his own blood instead of donor's blood, so there is no risk of contracting outside diseases. RBC washing devices can help remove byoproducts [9] in salvaged blood such as activated cytokines, anaphylatoxins, and other waste substances. These devices are used frequently in cardiothoracic and vascular surgery, in which blood usage has been high, traditionally [8]. We have reported recently the evidence for cell salvage procedure on cytokine induction, and advantages gained by using blood salvage procedure in reoperative surgery patients [10]. Because the blood is recirculated, there is no limit for the amount of blood that can be given back to the patient's circulation.

The purpose of this study is to compare blood loss in primo- and reoperative surgery patients and benefit from the cell salvage procedure in patients with excessive risk of perioperative bleeding. The clinical part of the study focuses on their relation to the outcomes: need for blood components transfusion, frequency of atrial fibrillation, tracheal intubation time and immediate postoperative course. In this subpopulation of patients blood salvage procedure is of great interest since they are of older age, they spend long time on antiplatelet therapy and they have numerous comorbidities. This would help in preparing patients for surgery with an increased risk of bleeding and to prevent postponing the surgical procedures.

Patients and Methods

Patients

Fifty-four patients with coronary artery disease scheduled for CABG and for the reoperative surgery (redo CABG) were included in this study. The patients entered the study from November 2010 until May 2011 at the Cardiovascular Institute Dedinje, Belgrade, Serbia. After ethical commitee aproval No 3710/2010 and written informed consent, patients were identified from the daily surgical programme. Final confirmation was obtained in the operating room during surgical

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procedure. Patients were divided into two groups: Group 1, the primary surgical revascularization (CABG) and Group 2, reoperative surgery on the coronary arteries (redo CABG). The inclusion criteria comprised the patients in need of simultaneous carotid artery endarterectomy (EAC). We excluded patients who had an indication for urgent intervention, as well as patients who needed valve replacement only. During the surgery there were two patients with changed indications, and they were excluded from further observation. Patients were monitored daily until they left the hospital. Any change in clinical status and the course of disease was monitored and recorded in the patients` record.

Study design

This was a prospective observational study. The basic tests included clinical data and routine laboratory blood tests. Blood samples were collected: 24 h prior, 6 h and 24 h after operation. The number of leukocytes, erythrocytes, platelets, haemoglobin and other haematological parameters were determined on an automatic haematology analyzer Coulter HMX counter (Beckman Coulter Electronics, Fullerton, USA). Perioperative bleeding was defined as an absolute fall in hematocrit immediately after surgery compared with preoperative values. The post-operative transfusion protocol was: in case of hemoglobin lower than 80 g/L or hematocrit lower than 25 % require blood transfision [11]. An additional hematocrit measurement was used upon discharge if no blood product have been used during the entire hospital stay.

Cell Salvage device (Dideco, Sorin, Italy) has been used as a routine procedure for many years in our hospital, and autologous blood transfusion provided safe blood. The day before and during open heart surgery we analyzed patients`coagulation and haemostatic status to optimize the need for transfusion, either allogenic or autologous blood products. Multiple electrode aggregometry (MEA) was done on Multiplate Platlet function analyzer (Dynabyte, Garmany) based on the principle that blood platelets are non-thrombogenic in their resting state, but expose receptors which allow them to attach on vascular injuries and artefitial surfaces. The platelet functions are tested by adding agonists of collagen (COL test) and trombin like peptid (TRAP test). In case that patient recieved antiplatelet agents until the operation we used aspirin agonists (arachidonic acid, ASPI test) and for clopidogrel adenosine difosfate (ADP test). Perioperatively was performed rotational thromboelastometry, Rotem (Pentapharm, Germany). Rotem is modified method of the tromboelastography, which explores perioperative activity of the coagulation plasma factors. There were several agonists examined: extrinsic way, tissue factor (Ex-tem), intrinsic way (In-tem), fibrinogen activity (Fib-tem) and fibrinolitic activity (Ap-tem).

Short-term follow-up period

We have analyzed the factors related to blood loss and clinical outcomes. The primary objective of the study was to determine the amount of drained blood and to compare it with defined clinical outcomes: blood substituted with autologous or allogenic erythrocytes, compensation of the blood products, the incidence of atrial fibrillation (AF) rate, revisions, tracheal intubation time, length of stay at the ICU, overall hospital stay, and survival. In the history of disease we entered all data about the transfusion of blood products, the volume of erythrocytes saved, the amount of units of blood products washed and returned, and the need for allogenic blood transfusions.

Statistical analyses

Statistical analyses were done using SPSS 11.0 software (SPSS, Chicago, IL). Data were presented as mean ± standard deviation (mean ± SD). Differences within the group and between two groups of haematological, biochemical and other clinical data were examined with analysis of variance (ANOVA). Proportions were compared using Student's t-test with the expected frequency less than five. Statistical significance has been accepted when p was <0.05. Correlation was shown as 95% Confidence Interval.

Results

Study population and study design

In this study patient population consisted of 44 male (84%) and 8 females (16%), with the average age of 61.5 ± 7.8 (range, 50-80) years. Isolated CABG surgery and first open heart surgery was performed in 30 patients (55%), reoperative surgery coronary artery surgery in 10 patients (19%), reoperative surgery coronary artery surgery with simultaneous carotid endarterectomy in 2 patients (4%), while 10 (22%) patients underwent combined CABG reoperative surgery and valvular surgery (Figure 1).

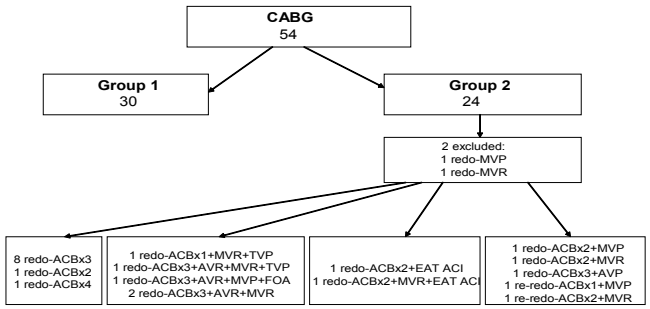

Figure 1: Patients profile. ACB=aortocoronary bypass; AVP=aortal valve plastic; AVR=Aortal Valve Replacement; CABG=Coronary Artery Bypass Grafting; EAT ACI=endarterectomy Arterie Carotis Interne; FOA=Foramen Ovale Apertum; MVP=Mitral Valve Plastic; MVR=Mitral Valve Replacement; TVP=Tricuspidal Valve Plastic; redo=reoperation; re-redo=re reoperation.

Variable	CABG (n=30)	redo CABG (n=22)	*p*-Value
Sex (male %)	23 (83.3%)	18 (81.8 %)	0.887
Age (years)	61.50 ± 7.7	65.95 ± 7.3	0.041
EuroSCORE	4.67 ± 1.373	8.00 ± 2.390	0.000
LVEF %	26.00 ± 4.80	35.64 ± 10.81	0.001
Body weight (kg)	79.89 ± 11.18	79.52 ± 14.54	0.922
Hypertension	24 (85.7%)	18 (81.8%)	0.899
Hyperlipidaemia	22 (78.6%)	14 (63.6%)	0.695
Diabetes mellitus	8 (28.6%)	5 (16.7%)	0.275
Smoking history	18 (62.1%)	14 (63.3%)	0.840
Aspirin therapy (%)	28 (93.3%)	17 (77.3 %)	0.094
Hemoglobin (g/L)	133.37 ± 16.1	137.0 ± 17.2	0.448
Leukocytes×10^9/L	8.05 ± 2.19	7.39 ± 3.23	0.390
Platelets×10^9/L	241.48 ± 67.55	186.86 ± 45.32	0.002
Number of bypass grafts	3.1 ± 0.84	2.59 ± 0.73	0.024
Cross-clamp time (min)	50.53 ± 14.53	78.09 ± 33.74	0.001
CPB (min)	82.83 ± 21.43	127 ± 57.93	0.002

Table 1: Characteristics of the patients for groups CABG and reoperative surgery CABG

Data are mean ± standard deviation for continue variables or n (%) for categorical variables.

Legend: CABG=Coronary Artery Bypass Grafting; LVEF=Left Ventricle Ejection Fraction; Redo CABG=reoperative surgery coronary artery bypass; CPB=cardiopulmonary bypass.

Variable	CABG (n=30)	redo CABG (n=22)	*p*-Value
Hemoglobin (g/L)	104.31 ± 10.12	114.00 ± 13.43	0.000
Leukocytes×10^9/L	17.07 ± 3.72	16.35 ± 4.71	0.000
Platelets×10^9/L	155.04 (126.83-189.51)	131.00 (113.57-151.10)	0.165
AF (%)	5 (16.7%)	3 (13.6%)	0.765
Tracheal intubation time (hours)	16.073 (13.99-18.45)	19.120 (12.13-30.11)	0.453
Revision (%)	3 (10.0%)	2 (9.1%)	0.913
Blood loss (ml)	868.52 ± 587.555	1088.33 ± 819.517	0.285
Length of stay at ICU (days)	3.032 (2.327-3.951)	4.555 (2.762-7.513)	0.145
Length of stay at hospital (days)	9.141 (7.973-10.479)	14.606 (10.226-20.863)	0.017

Table 2: Laboratory findings and clinical outcomes after CABG primo- and reoperative surgery

Data are mean ± standard deviation for continue variables or n (%) for categorical variables. Lab data are taken 24 hours after operations.

Legend: AF=Atrial Fibrillation Rate; CABG=Coronary Artery Bypass Grafting; ICU=Intensive Care Unit; Redo CABG=reoperative surgery coronary artery bypass.

Transfused products (ml)	Mean ± SD		
	CABG	redo CABG	p-Value
Packed red blood cells transfused intraoperatively	505.5 ± 169.4	556.6 ± 332.0	0.61
Autologous erythrocytes reinfusad intraoperatively	566.0 ± 146.6	733.4 ± 297.7	0.05
Fresh frozen plasma transfused	906.5 ± 452.8	829.1 ± 289.0	0.68
Crioprecipitate substitution	400.0 ± 142.2	440.0 ± 242.2	0.89
Packed red blood cells transfused postoperatively	771.1 ± 809.5	1143.0 ± 958.7	0.32
Platelets transfused	466.6 ± 378.6	502.0 ± 292.2	0.88

Table 3: Blood products substituted in Group 1 and Group 2.

Legend: CABG=Coronary Artery Bypass Grafting; Redo CABG=reoperative surgery coronary artery bypass.

Baseline characteristics of patients, laboratory data and intraoperative factors in both groups were summarized in Table 1. In Group 2 only 4/22 (18%) patients were on therapy with clopidogrel. Total heparin dose was 7.8 ± 3.2 mL and total protamine dose was 337 ± 65 mg, measured during reoperative CABG surgery.

Clinical endpoints

The groups observed showed no statistically significant difference in clinical outcomes (Table 2), except for the length of hospitalization. Only one patient died in the Group 2, survival rate was 21/22 (95.45%) in reoperative surgery, and 100% in primo-operated patients. Although there was some difference in the amount of blood drained from the operative field, it is statistically insignificant (p=0.285). ICU stay and mortality rates were not statistically different, but the time spent in hospital until discharge was significantly longer in reoperative surgery patients (0.017). In both groups positively correlated were: duration of the cardiopulmonary bypass (CPB), the aortic clamping time and the amount of drained blood content, but without statistical significance. On the other side, in both groups a negative correlation was found between ICU stay and LVEF (Group 1 r=-0.14; p=0.56 *vs.* Group 2 r=-0.13; p=0.55). There was a positive correlation with a statistical significance between length of stay at the ICU and a Euroscor (r=0.59, p=0.004), time on the CPB (r=0.53, p=0.012) and the drainage r=0.49 (p=0.021). Observing the relationship between length of stay at the ICU and patient's age they are in positive correlation (r=0.27, p=0.2), but do not reach the level of significance.

As laboratory parameters measured postoperatively show in Table 2, there was no difference between Group 1 and Group 2, except for the content of haemoglobin and white blood cells count. Since the re-exploration increased the tendency of bleeding, the contributing factors and their relations are shown in Table 3. Only 1/22 (4.5%) patient in Group 2 had postoperative Rotem-analysis which was not suitable.

Of 52 patients observed, 27 patients (51.92%) received a blood transfusion. In the Group 1, 19 (63%) patients received alloproducts: 18 (60%) intraoperatively, 13 (43%) postoperatively, and 12 (40%) patients received alloproducts during and after surgery (Table 3). In the Group 2, 13 (59%) patients received alloproducts: 9 (40%) intraoperatively, 4 (18%) postoperatively, and 13 (59%) patients during and after surgery. In the Group 1, 15 (50%) patients received their own erythrocytes, while in the Group 2, blood were collected and returned to peripheral circulation in 17 (77%) patients.

Preoperative clopidogrel and aspirin use (p=0.09) was not statistically different. Platelet count lower than 50% has been seen intraoperatively in only 6/22 (27.7%) of the reoperative surgery patients. However, platelet count was lower preoperatively while hemoglobin amount was significantly lower postoperatively (p=0.00) in reoperative CABG surgery. Although we found some difference in blood volume drained (868.5 ± 587.5 *vs.* 1040 ± 823.4 mL) it was not statistically relevant (p=0.28). Allogenic erythrocytes substituted intraoperatively were not statistically different (p=0.61), while autologous blood returned after cell salvage procedure was higher in the Group 2 (p=0.05). Platelets transfused (p=0.88), fresh frozen plasma (p=0.68), and packed red blood cells transfused postoperatively (p=0.32) have not reached statistical significance. The length of stay at the ICU was not influenced by used blood components transfusion, either allogeneic or autologous.

The positive correlation between blood loss and ICU stay (r=0.49, p=0.021) in reoperative CABG surgery patients is shown in Figure 2.

Discussion

Intraoperative blood salvage is a medical procedure which involves recovering of blood lost during surgery and re-infusing it into the pacient [12]. Primary research goal was to determine whether the patients undergoing complicated surgery have a higher degree of blood

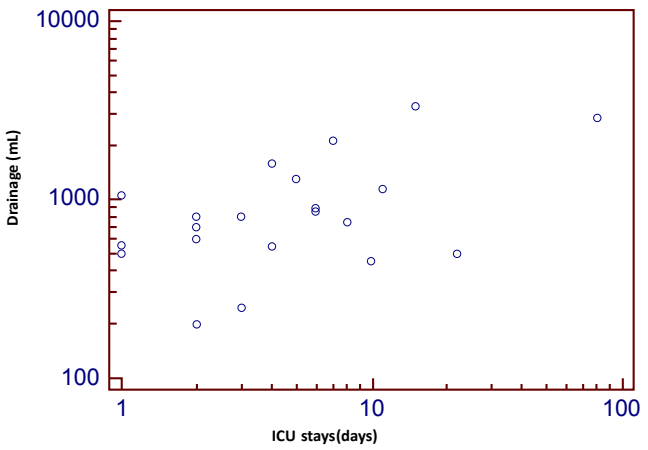

Figure 2: Positive correlation between blood loss and length of ICU stay was found in reoperative surgery patients (r=0.49, p=0.021).

Legend: ICU=Intensive Care Unit.

loss during and after the surgery and to investigate by which extent cell salvage procedure reduces the risk of perioperative bleeding.

Antiplatelet therapy is the cornerstone in treatment of patients with coronary artery disease. Open heart surgery, by using CPB, additionally compromises the hemostasis. Approximately 4% of patients require reoperation due to hemorrhage [3,11,12] which is associated with increased mortality and morbidity [6]. Woodman and co-workers found that almost 5% of patients receive more than 10 units of perioperative blood transfusion [4]. CPB induces the alterations in the haemostatic system, leading to excessive activation of coagulation and fibrinolytic pathways with complex interactions between cellular and soluble inflammatory systems [10-12]. The hypothermia and hemodilution further complicate the situation. The use of whole blood impedance aggregometry and rotational thromboelastometry can reveal useful data about platelet function and viscoelastic properties of blood clots in patients undergoing cardiac surgery. After institution of blood management program and thromboelastography in cardiac surgical patients, Spies and co-workers stated that the potential risk of re-exploratory hemorrhage was reduced from 5.7% to 1.5% of monitored patients [13]. Pathophysiologically, the balance between bleeding, normal hemostasis, and thrombosis is markedly influenced by the rate of thrombin formation and platelet activation. There is recent evidence that genetic variability modulates the activity in each of these mechanistic pathways [14].

In our study approximately 10% of patients were revised immediately after the surgery and one of them died, having the highest preoperative risk and numerous comorbidities. Need for blood transfusion in our study was similar as it was reported by other authors [1,2,11]. We included patients with low left ventricular ejection fraction (26% *vs.* 35%, p=0.001) to form adequate control group (Group 1) for complicated cardiac surgery (Group 2). Patients in these groups did not differ by sex and weight, but the basic preoperative characteristics were different. Patients from Group 2 belonged to an older age (66 ± 7, range 55-80 years) (p=0.041), because the reoperative surgery was preceded by a period of one year or more, from the first surgery. They also had a higher preoperative risk assessment for cardiac intervention, estimated by EuroSCORE system ((p<0.000). Reoperative surgery is generally a high-risk surgery [15].

Taken together laboratory parameters measured preoperatively, significant differences were found in haematological values, precisely in platelet count (p=0.002). It did not affect the clinical course and outcome because they were within the reference range recommended for adult population in both groups, although with lower values in patients on reoperative surgery at the start of the study. Analyzing intraoperative factors related to bleeding, aortal-clamping time (p=0.001) and CPB duration (p=0.002) were longer in Group 2. Number of bypass grafts (p=0.024) were significantly lower in those patients, but they had combined procedures. We should consider the type of surgery, where more than half of the reoperative surgery patients have had coronary artery bypass along with carotid artery or valve reconstructions.

When we look at the clinical course immediately after the operation, no difference has been seen in the number of revisions, time on mechanical ventilation and incidence of atrial fibrillation. In patients with reoperative surgery hospital stay was longer, but in accordance with experience from Goodman et al. [16]. The explanation for this could be that the strategy which improves biocompatible materials of the circuit reduces the incidence of complement activation, which reduces post-operative complications, especially in high-risk patients [17]. Several authors referred that significant reduction of myocardial injury, blood loss and the patient's cognitive sequels initiated by the CPB could be diminished by cell salvage procedures [18]. No differences were found in haemoglobin levels before open heart surgery in the two groups of patients (133.3 ± 16.1 g/L *vs.* 137.0 ±17.2; 0.44), but the Group 2 of patients had significant improvement in haemoglobin level after the infusion of processed blood (104.3 ± 10.2 *vs.* 114.0 ± 13.3 g/L; 0.00). In observed groups neither the quantity of blood drained, nor substituted allogeneic blood products given preoperatively were different. On the contrary, the use of cell saver helped to reduce the need for allogenic blood transfusion. The Group 2 of patients had increased amount of the autologous RBC transfusions (566.0 ± 46.6 *vs.* 733.4 ± 297.8; 0.05) what could be an explanation for the increased haemoglobin levels in reoperated patients. Based on our previous report, we believe that the degree of inflammation caused by the CPB had no effect on clinical outcomes in patients with reoperative surgery, partially because of the intraoperative cell salvage procedure [10]. In addition, the thromboelastometry and MEA measurement before and during open heart surgery are helpful in the case of using double pharmacotherapy, by aspirin and clopidogrel. This would help in preparing patients for surgery with an increased risk of bleeding and to prevent postponing of surgical procedures.

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