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# Hematological Changes in Patients Undergoing Coronary Artery Bypass Surgery: a Prospective Study

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## ABSTRACT

**Objectives:** Removal of pro inflammatory stimuli after CABG, wound closure and the regenerative ability of the bone marrow will ensure a gradual recovery of hematological parameters. The aim of this study was to assess the hematological changes after CABG. **Materials and Methods:** A prospective cohort study included 164 consecutive patients undergoing on pump CABG surgery between January 2012 and January 2013. Patients with primary hematologic disease, emergent or urgent CABG and off-pump CABG were not included. A time line protocol was employed. **Results:** All patients survived surgery. Average values of erythrocytes, hemoglobin and hematocrit declined, to reach lower values on day 3 after surgery (-33.6 %, -33.1 %, -32.6 % versus preoperative value,  $p < 0.001$ ) and then gradually increased to reach normal values after one month and the preoperative values after three months. The average values of leukocytes and neutrophils increased rapidly to achieve the highest value on day 2, while the average value of lymphocytes decreased quickly to achieve lower value on day 1 after surgery (+74.7 %, +127.1 %, -52.4 % respectively from the preoperative value,  $p < 0.001$ ). The average platelet count decreased to the lowest value on day 2 after surgery (-26.4 % from the preoperative value,  $p < 0.001$ ), after which gradually increased up to +100.8 % of preoperative value on day 14 ( $p < 0.001$ ) and then gradually decreased to reach normal values on day 21 and preoperative values after three months. **Conclusions:** Average values of the three peripheral blood cells parameters undergo important changes after CABG, but not life threatening, and regain normal and preoperative values after 1-3 months after surgery.

**Key words:** Peripheral blood, Cardiac surgery, Coronary artery bypass grafting, Regenerative.

## 1. INTRODUCTION

Major surgery and in particular cardiac surgery is a challenge to the hematopoietic system. The use of Cardiopulmonary Bypass (CPB), bleeding (during and after surgery), frequent blood analyses (before, during and after surgery), hemodilution, significant shift of intravascular volume, mechanical trauma of blood cells, therapeutic hypothermia, co-morbidities, the use of anticoagulant and antiplatelet drugs (before, during and after surgery), transfusion of blood products, cause significant changes in the three major cellular components of the hematopoietic system (1). Experience and literature have shown that the values of peripheral blood parameters (number, size, function) undergo significant changes during the early phase of the surgery, gradually recovery during the postoperative period and reach the preoperative (baseline) values 2-6 months after surgery (2). Removal of pro inflammatory stimuli after surgery, wound closure and

the regenerative ability of the bone marrow will ensure a gradual recovery to preoperative values of the hematological parameters. The aim of this study was to assess the hematological changes after artery bypass graft surgery (CABG).

## 2. METHODS

Between January 2012 and January 2013, 164 consecutive patients (138 men and 26 women) underwent elective CABG surgery at our division of cardiac surgery. The study received the IRB agreement. This cohort of patients was prospectively evaluated. Patients with primary hematologic disease were not included in the study. Patients undergoing emergent surgery or off-pump CABG were not included in this study. All patients were operated by the same surgeon.

Patients were reviewed for their preoperative demographic, clinical (coronary artery disease severity and

co-morbidities) and laboratory variables and then followed to record their postoperative data and outcomes.

Day 0 was the day of surgery. Hematological parameters were assessed before surgery (D-1) and after surgery: at the first day (D+1); the second day (D+2), the patient was transferred from the intensive care unit to the ward; the third day (D+3); the fourth day (D+4); the sixth day (D+6), the patient left the hospital; at the end of the second week (D+14), the third week (D+21), the fourth week (D+28) and the twelfth week (D+90).

To achieve a complete blood count analysis, 4 ml of venous blood was taken by venipuncture technique, by Vacutest REF 13030 K3 EDTA 7.2 mg, and evaluation done on the equipment Sysmex XS-1000i Automated Hematology Analyzer.

The purpose of this study was to assess changes in hematological parameters of peripheral blood after cardiac surgery (the count of red blood cell, leukocytes, neutrophils, lymphocytes, platelets and the values of haemoglobin, hematocrit, MPV), analyzing changes in trend over time until 90 days after cardiac surgery and comparison with values before surgery.

All patients included in the study were managed according to the hospital's current policies regarding preoperative preparation, intraoperative surgical and anesthetic management and postoperative care.

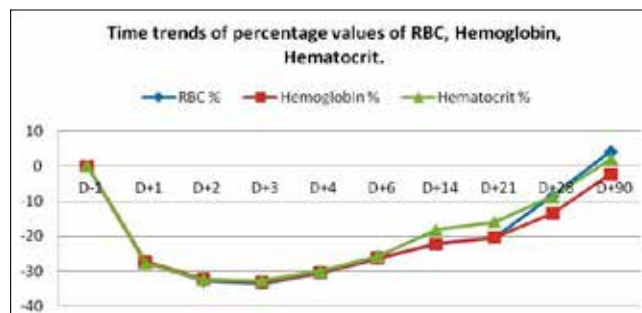
All cardiac medications were continued until the day of surgery, except antiplatelet drugs, which were stopped 5 days prior to surgery in elective patients. Anesthetic technique was standardized in all patients. Patients were premedicated with 7.5 mg Midazolam orally the night before surgery and 10 mg morphine intramuscularly 30 minutes before they were sent to the operating theatre. Anesthesia was induced with 0.05–0.1 mg/kg Midazolam, 5–10 µg/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 as vasodilators, dobutamine and dopamine as inotropes, and noradrenaline and adrenaline as vasopressors. All surgical procedures, i.e., on-pump and off-pump, were performed via median sternotomy.

Packed red blood cells (RBC) were transfused according to the needs of each patient. Blood transfusion was used to maintain Hematocrit (Hct) > 25% and hemoglobin (Hb) > 8.5 g/dL during cardiac surgery.

Activated clotting time (ACT) was measured before surgery. All on-pump patients required 2g tranexamic acid as an antifibrinolytic agent at the start of anesthesia. The anticoagulation was achieved with an initial dose of 300 U/kg heparin injected into the central venous system with ACT > 400 seconds (3–5 minutes after administration of heparin). At the end of the bypass procedure, the effect of heparin was reversed with protamine chloride at a ratio of 1:1. Platelet count and homeostasis test were

Age, years	61.8 ± 9.0
Males/Females	138/26
Weight, kg	79.0 ± 11.4
Body surface area, m <sup>2</sup>	1.9 ± 0.1
Body mass index, kg/m <sup>2</sup>	26.9 ± 3.4
Diabetes Mellitus, %	43.2
Hypertension, %	72.5
Dyslipidemia, %	17.6
Heritage, %	10.3
Smoking, %	22.0
Alcohol, %	8.5
Red blood cells, mm <sup>3</sup>	4590609.7 ± 596768.0
Hemoglobin, gr/dl	13.4 ± 1.6
Hematocrit, %	40.0 ± 4.7
Mean corpuscular volume, fL	87.0 ± 6.0
Mean corpuscular hemoglobin, pg	29.4 ± 2.3
Red blood cell distribution, %	13.71 ± 2.2
White blood cells, mm <sup>3</sup>	8305.7 ± 2207.5
Neutrophils, mm <sup>3</sup>	5058 ± 1846
Lymphocytes, mm <sup>3</sup>	2273.5 ± 744.6
Platelets, mm <sup>3</sup>	230920.7 ± 65064.7
Mean platelet volume, fL	10.6 ± 1.1
Neutrophil-lymphocyte ratio	2.4 ± 1.5
Platelet-lymphocyte ratio	111.1 ± 45.0
Preoperative Anemia, %	29.2

**Table 1.** Preoperative demographics and hematologic data.



**Figure 1.** Time trends of percentage values of Red blood cells, Hemoglobin, Hematocrit.

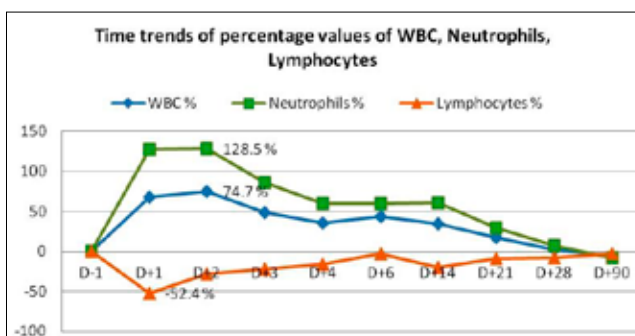
carried out after heparin antagonization. Mean arterial blood pressure was maintained at 50–70 mmHg.

We used autologue 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. Patients were transferred to the ICU, intubated, and mechanically ventilated until they were ready to be awoken.

Statistical Methods: Group statistics were expressed as mean ± SD. The paired-sampled t test Bonferroni was performed for the statistical analysis between groups. Significance between data was considered achieved when  $p < 0.05$ . SPSS 20.0 software (IBM, 2011) was used for statistical analysis.

	Preoperative RB-C $\pm$ SD, mm <sup>3</sup>	Postoperative RB-C $\pm$ SD, mm <sup>3</sup>	t	p	Preoperative Hg $\pm$ SD, gr/dl	Postoperative Hg $\pm$ SD, gr/dl	t	P	Preoperative Hct $\pm$ SD, %	Postoperative Hct $\pm$ SD, %	t	P
D-1;D+1	4590609.7 $\pm$ 596768	3328628 $\pm$ 487111.2	21	<0.001	13.4 $\pm$ 1.6	9.8 $\pm$ 1.3	22.36	<0.001	40 $\pm$ 4.7	28.9 $\pm$ 3.7	23.76	<0.001
D-1;D+2	4590609.7 $\pm$ 596768	3086375 $\pm$ 387076.5	27.7	<0.001	13.4 $\pm$ 1.6	9.1 $\pm$ 1	29.2	<0.001	40 $\pm$ 4.7	27 $\pm$ 3.1	29.57	<0.001
D-1;D+3	4590609.7 $\pm$ 596768	3050191 $\pm$ 466538.6	26	<0.001	13.4 $\pm$ 1.6	9 $\pm$ 1.2	28.17	<0.001	40 $\pm$ 4.7	26.9 $\pm$ 3.5	28.63	<0.001
D-1;D+4	4590609.7 $\pm$ 596768	3184870.1 $\pm$ 473869.1	23.63	<0.001	13.4 $\pm$ 1.6	9.3 $\pm$ 1.2	26.25	<0.001	40 $\pm$ 4.7	28.0 $\pm$ 3.7	25.7	<0.001
D-1;D+6	4590609.7 $\pm$ 596768	3377151.9 $\pm$ 437229.3	35.54	<0.001	13.4 $\pm$ 1.6	9.9 $\pm$ 1.0	23.76	<0.001	40 $\pm$ 4.7	29.7 $\pm$ 3.2	23.2	<0.001
D-1;D+14	4590609.7 $\pm$ 596768	3575625 $\pm$ 527160.6	16.33	<0.001	13.4 $\pm$ 1.6	10.4 $\pm$ 1.4	18	<0.001	40 $\pm$ 4.7	32.7 $\pm$ 3.7	15.63	<0.001
D-1;D+21	4590609.7 $\pm$ 596768	3653428.5 $\pm$ 490113.6	15.7	<0.001	13.4 $\pm$ 1.6	10.7 $\pm$ 1.4	16.26	<0.001	40 $\pm$ 4.7	33.6 $\pm$ 3.6	13.84	<0.001
D-1;D+28	4590609.7 $\pm$ 596768	4203658.5 $\pm$ 589519.9	5.91	<0.001	13.4 $\pm$ 1.6	11.6 $\pm$ 1.6	10.2	<0.001	40 $\pm$ 4.7	36.5 $\pm$ 4.6	6.8	0.003
D-1;D+90	4590609.7 $\pm$ 596768	4790303 $\pm$ 473117.8	3.36	<0.001	13.4 $\pm$ 1.6	13.1 $\pm$ 1.5	1.75	0.081	40 $\pm$ 4.7	40.8 $\pm$ 4.2	1.6	0.11

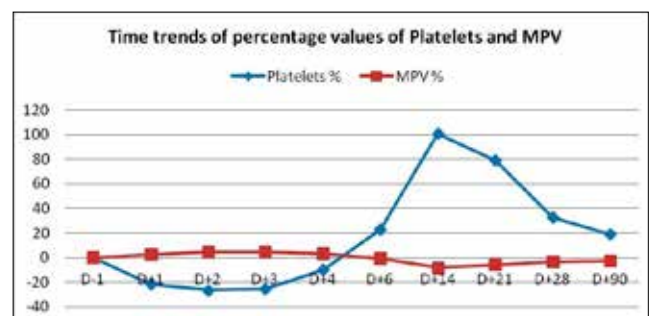
**Table 2.** Comparison with preoperative values (D-1)  $\pm$  Standard Deviation (SD), for Red blood cells, Hemoglobin and Hematocrit. Legend: RBC-Red Blood Cells, Hct-Hematocrit, Hg-Hemoglobin, SD-Standard deviation



**Figure 2.** Time trends of percentage values of White blood cells, Neutrophils, Lymphocytes.

### 3. RESULTS

The mean age of the patients was  $61.8 \pm 9.0$  years (range, 34-82 years). The preoperative demographics and hematology data are presented in Table 1. Time trends of the average values of RBC (mm<sup>3</sup>), Hb (gr/dl), and Hct (%), Standard Deviation (SD), percentage changes of these values versus D-1 (preoperative value taken as the basic value) are presented in Figure 1. Comparison with preoperative values of erythrocytes (D-1)  $\pm$  Standard Deviation (SD) for pairs: D-1, D+1; D-1, D+2; D-1, D+3; D-1, D+4; D-1, D+6; D-1, D+14; D-1, D+21; D-1, D+28; D-1, D+90; are presented in the Table 2. The same univariate analysis was employed for the Hb level, and Hct level (Table 2) postoperatively versus preoperatively. Average values of RBC, Hb and Hct declined to reach their lower values on day 3 after surgery (-33.6 %, -33.1 %, -32.6 % respectively from the preoperative value,  $p < 0.001$ ) and then gradually increased to reach normal values after one month and the preoperative values after three months. Time trends



**Figure 3.** Time trends of percentage values of Platelets and Mean platelet volume.

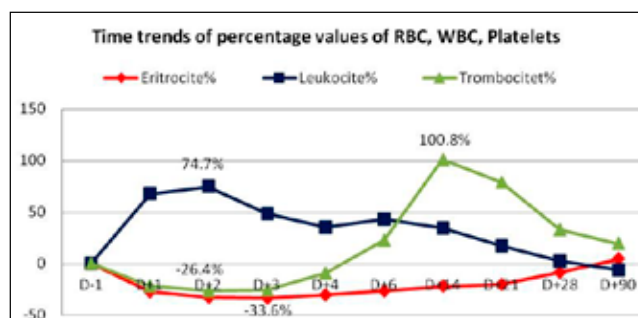
of the average values of white blood cells (WBC) (mm<sup>3</sup>), Neutrophils (mm<sup>3</sup>), Lymphocytes (mm<sup>3</sup>) and SD, percentage changes of these values versus D-1 (preoperative value taken as the basic value) are presented in Figure 2. Comparison with preoperative values of WBC (D-1)  $\pm$  SD for pairs: D-1, D+1; D-1, D+2; D-1, D+3; D-1, D+4; D-1, D+6; D-1, D+14; D-1, D+21; D-1, D+28; D-1, D+90; are presented in the Table 3. The same univariate analysis was employed for the neutrophils and lymphocytes postoperatively versus preoperatively (Table 3). The average values of leukocytes and neutrophils increased rapidly (neutrophil leukocytosis) to achieve the highest value on day 2 after surgery, while the average value of lymphocyte decreased quickly to achieve lower value on day 1 after surgery (+74.7 %, +127.1 %, -52.4 % respectively from the preoperative value,  $p < 0.001$ ). Once these values were reached the average values of leukocytes and neutrophils were reduced gradually and the average value of lymphocytes increased gradually to reach the normal levels on day 21 and the preoperative values on day 28.

	Preoperative WBC $\pm$ SD, mm <sup>3</sup>	Postoperative WBC $\pm$ SD, mm <sup>3</sup>	T	P	Preoperative Neutrophile $\pm$ SD, mm <sup>3</sup>	Postoperative Neutrophile $\pm$ SD, mm <sup>3</sup>	T	P	Preoperative Lymphocytes $\pm$ SD, mm <sup>3</sup>	Postoperative Lymphocytes $\pm$ SD, mm <sup>3</sup>	t	P
D-1;D+1	8305.7 $\pm$ 2207.5	13912.3 $\pm$ 4086.6	15.46	<0.001	5058.8 $\pm$ 1846	11493.4 $\pm$ 3858.7	19.26	<0.001	2273.5 $\pm$ 744.6	1081.2 $\pm$ 588.4	16.1	<0.001
D-1;D+2	8305.7 $\pm$ 2207.5	14509.5 $\pm$ 4205.9	16.73	<0.001	5058.8 $\pm$ 1846	11560.8 $\pm$ 3851.1	19.5	<0.001	2273.5 $\pm$ 744.6	1636.2 $\pm$ 713	7.9	<0.001
D-1;D+3	8305.7 $\pm$ 2207.5	12317.7 $\pm$ 3838.9	11.6	<0.001	5058.8 $\pm$ 1846	9426.2 $\pm$ 3585.2	13.9	<0.001	2273.5 $\pm$ 744.6	1765.8 $\pm$ 760.9	6.1	<0.001
D-1;D+4	8305.7 $\pm$ 2207.5	11227.7 $\pm$ 3720.1	8.65	<0.001	5058.8 $\pm$ 1846	8081.7 $\pm$ 3321	10.2	<0.001	2273.5 $\pm$ 744.6	1909.9 $\pm$ 873.2	4.06	<0.001
D-1;D+6	8305.7 $\pm$ 2207.5	11893.5 $\pm$ 3439.5	11.24	<0.001	5058.8 $\pm$ 1846	8053.9 $\pm$ 2930.1	11.08	<0.001	2273.5 $\pm$ 744.6	2216.3 $\pm$ 921.9	0.62	0.54
D-1;D+14	8305.7 $\pm$ 2207.5	11155.6 $\pm$ 3278.3	9.23	<0.001	5058.8 $\pm$ 1846	8114.2 $\pm$ 2942.4	11.26	<0.001	2273.5 $\pm$ 744.6	1815.2 $\pm$ 695.3	5.76	<0.001
D-1;D+21	8305.7 $\pm$ 2207.5	9744.4 $\pm$ 3105.4	4.8	<0.001	5058.8 $\pm$ 1846	6548.5 $\pm$ 2788.7	5.7	<0.001	2273.5 $\pm$ 744.6	2072.1 $\pm$ 1063.1	2	0.048
D-1;D+28	8305.7 $\pm$ 2207.5	8506.3 $\pm$ 1899.0	0.88	0.38	5058.8 $\pm$ 1846	5433.9 $\pm$ 1934.6	1.93	0.055	2273.5 $\pm$ 744.6	2091.5 $\pm$ 718.1	2.25	0.025
D-1;D+90	8305.7 $\pm$ 2207.5	7796.3 $\pm$ 2143.1	2.12	0.035	5058.8 $\pm$ 1846	4653.3 $\pm$ 1670.5	2.08	0.038	2273.5 $\pm$ 744.6	2199.8 $\pm$ 745.4	0.9	0.37

**Table 3.** Comparison with preoperative values (D-1)  $\pm$  Standard Deviation (SD), for White blood cells, neutrophils, and lymphocytes. Legend: WBC-White Blood Cells, SD- Standard deviation

	Preoperative Platelets±SD, mm <sup>3</sup>	Postoperative Platelets±SD, mm <sup>3</sup>	t	P	Preoperative MPV±SD, fl	Postoperative MPV±SD, fl	t	P
D-1;D+1	230920.7 ± 65064.7	180792.6 ± 67375.4	6.85	<0.001	10.6 ± 1.1	10.9 ± 1.1	2.47	0.014
D-1;D+2	230920.7 ± 65064.7	169956.2 ± 66796.4	8.37	<0.001	10.6 ± 1.1	11.1 ± 1.2	3.93	<0.001
D-1;D+3	230920.7 ± 65064.7	171762.8 ± 66144.8	8.17	<0.001	10.6 ± 1.1	11.1 ± 1.2	3.93	<0.001
D-1;D+4	230920.7 ± 65064.7	208928.5 ± 76582.7	2.8	0.005	10.6 ± 1.1	10.9 ± 1.2	2.36	0.019
D-1;D+6	230920.7 ± 65064.7	283528.6 ± 94593.9	5.9	<0.001	10.6 ± 1.1	10.5 ± 1.2	0.79	0.43
D-1;D+14	230920.7 ± 65064.7	463762.5 ± 143604	18.9	<0.001	10.6 ± 1.1	9.7 ± 1.1	7.4	<0.001
D-1;D+21	230920.7 ± 65064.7	413181.8 ± 159701.1	13.54	<0.001	10.6 ± 1.1	10.0 ± 1.1	4.9	<0.001
D-1;D+28	230920.7 ± 65064.7	307200.0 ± 85383.3	9.1	<0.001	10.6 ± 1.1	10.3 ± 1.1	2.47	0.014
D-1;D+90	230920.7 ± 65064.7	275514.3 ± 113725.7	4.4	<0.001	10.6 ± 1.1	10.3 ± 0.9	2.7	0.007

**Table 4.** Comparison with preoperative values (D-1) ± Standard Deviation (SD), for Platelets and mean platelet volume. Legend: MPV-Mean Platelet Volume, SD-Standard Deviation



**Figure 4.** Time trends of percentage values of Red blood cells, White blood cells, Platelets.

Time trends of the average values of Platelets (mm<sup>3</sup>) and mean platelet volume (MPV)(fL), Standard Deviation (SD), percentage changes of these values versus D-1 (preoperative value taken as the basic value) are presented in Figure 3. Comparison with platelet and MPV preoperative values are presented in the Table 4. The average platelet count decreased gradually to reach the lowest value on day 2 after surgery (-26.4 % from the preoperative value,  $p < 0.001$ ), after which gradually increased up to +100.8 % of the preoperative value on day 14 ( $p < 0.001$ ) and then gradually decreased to reach normal values on day 21 and preoperative values after three months. The average values of MPV change in inverse way according to the average values of platelets (in regenerative bone marrow response).

Time trends of the average values of RBC (mm<sup>3</sup>), WBC (mm<sup>3</sup>), Platelets (mm<sup>3</sup>), percentage changes of these values versus D-1 (preoperative value taken as the basic value) are presented in Figure 4. All the three peripheral blood cells parameters undergo changes after CABG. RBC get to their lower average value in D+3 (-33.6 % from the preoperative value); in D+2 leukocytes get to their higher average value (+74.7 % from the preoperative value), and the platelets to their lower average value (-26.4 % from the preoperative value). Leukocytes regain their normal level in D+21, erythrocytes and platelets regain their normal level in D+28. All three elements recover totally in their preoperative levels within three months (D+90).

#### 4. DISCUSSION

Systematic assessment of peripheral blood hematologic parameters after cardiac surgery is important for the assessment of their changes and correction. Anemia is a

major concern in patients undergoing CABG and may be present in over 90 % of cases (3) and it can be explained by acute blood loss during and after surgery. About 75-90% of intra-operative and early post-operative bleeding is associated with technical factors and due to CPB which is associated with hemodilution (4).

Anemia is associated with a range of postoperative consequences (stroke, acute myocardial infarction), major side effects, re-hospitalization, duration of stay in the Intensive Care Unit and hospital stay, mortality 30 days after the intervention (5). Westenbrink et al (6) noted that every 1 mg/dl decrease in Hb was associated with a 13% increase in cardiovascular events and 22 % increase in all-cause mortality. Van Straten et al (7) demonstrated that postoperative anemia is a risk factor for early and late mortality in patients undergoing CABG. The acute reduction in Hct produced a reversible platelet dysfunction, manifested by an increase in bleeding time (BT) and a decrease in the shed blood Thromboxane B2 level at the template BT site (8). Blood loss is a common problem in cardiac surgery, which requires some re-interventions, while massive blood loss (the replacement by transfusion of more than 5 units PRBC within 1 day of surgery) was associated with an 8.1-fold in the odds of death (9). Clinical studies emphasize the paradox that both anaemia and transfusion are associated with organ injury and increased morbidity and mortality across a wide span of disease states and surgical interventions (10).

Our study revealed that the prevalence of postoperative anemia was 100 %. There was mild anemia in 1.2 % of the cases; moderate anemia in 66.5 % and severe anemia in 32.3 % of the cases. 43.7% of the patients with severe anemia had preoperative anemia too.

Loor et al (11) evaluated that median nadir Hct was 30%. The lowest value of Hct is associated with renal function damage, more cardiac damages, longer hospitalization and higher mortality. Ranucci et al (12) noted that median values of the lowest Hct on CPB below 25 % were associated with an increased major morbidity rate. The lower average value of Hct in our study was 26.9 % in the third day after surgery.

Karkouti et al (13) demonstrated that a decrease of Hb concentration by 50% according to the basal value was independently associated with increased risk for adverse outcomes. Even in the absence of bleeding, intravascular fluid cause shifts in hemoglobin levels to drift postoper-



atively, possibly confounding the decision to transfuse. Tschakowsky et al (14) have shown that after cardiac surgery, by postoperative day 4, the circulating blood volume has reached its maximum and thus Hb levels reach their nadir. In our study, the average Hb level falls after surgery in 100 % of cases and reaches the lowest value (nadir) on day 3 (9.0 g/dL; 33.1 % decreases from preoperative level). After nadir, the average Hb level increases gradually and on day 6 patients exhibited hemoglobin recovery of  $0.98 \pm 1.27$  g/dL ( $p < 0.001$ ). The average Hb value regained the preoperative value in D+90 ( $p = 0.354$ ).

Santa Ursula et al (15) noted that at the end of cardiac surgery a marked and sustained leukocytosis was found. In the differential count there were significant increase in neutrophils, associated with band and immature forms, corresponding with significant reductions in lymphocytes. Leukocytosis is also very common after surgery and generally represents an acute response to the stress. The count of leukocytes and neutrophils increased significantly (neutrophilic leukocytosis) by the end of the surgery, until 24 hours thereafter. This rapid increase of the total count of leukocytes and neutrophils comes from the mobilization of the marginalized neutrophils and release of new neutrophils from bone marrow and the pulmonary circulation. The normal response to inflammation will be accompanied by an increase of leukocyte count, primarily to neutrophils and less mature forms (left shift). Acute bleeding (4-5), physical and emotional stress, anesthesia and drugs also increase circulating leukocytes (16). As a rule, it will improve in further measurements and if growth persists or occurs after a period of decline it is thought to be an infection.

The number of neutrophils markedly increases at the end of cardiac surgery and remains elevated for 48 hours (17). CPB induces a whole body inflammatory response that sometimes leads to postoperative organ dysfunction and neutrophil activation plays an important role in this reaction. Neutrophil activation is implicated in postoperative complications in patients having cardiac surgery with CPB (18). Leukocytosis was identified as an alarming sign for mortality among patients admitted to general hospital wards at early stages of admission (19). High WBC count before CABG surgery is an independent risk factor for ischemic events one year after the surgery (20). Activated neutrophils stimulate platelet activation. Close contact between platelets and neutrophils modulates their cellular interactions in thrombotic and inflammatory states, with stimulation of P-selectin expression on platelets by agonists such as thrombin and neutrophil-derived cathepsin G. Neutrophils enhanced aggregation of human platelets and neutrophil cathepsin G is a physiologic modulator of platelet thrombus formation in vivo (21).

Despotis et al (22) have demonstrated that patients who exhibit the greatest increase in WBC count during the course of CPB are most likely to bleed during the first 24 postoperative hours. On-site measurements of WBC count as an index of the inflammatory response to CPB may be useful in identifying patients at increased risk for excessive bleeding. By using this information physicians may be able to intervene with anti-inflammatory medications and blood preservation techniques.

In our study, the average values of leukocytes and neutrophils increased rapidly (neutrophil leukocytosis) to achieve the highest values on day 2 after surgery, while the average value of lymphocytes decreased quickly to achieve lower value on day 1 after surgery. 90.2% of the patients had neutrophilic leukocytosis after cardiac surgery; 98% of these patients had mild leukocytosis and 2% had moderate leukocytosis. The maximal level of the leukocytes was  $34.170 \text{ mm}^3$ . Once these values were reached, the average values of leukocytes and neutrophils were reduced gradually and the average value of lymphocytes increased gradually to reach the normal levels on day 21 and the preoperative values on day 28.

Postoperative thrombocytopenia associated with CABG is a common clinical condition. The relative decrease in platelet counts within the first 3 to 4 days after major surgery is informative about the magnitude of the trauma or blood loss, whereas the dynamic of the platelet count course thereafter shows whether or not the physiologic compensatory mechanisms are working. The platelet count nadir is typically reached by days 3 and 4 for major surgery and is nearly always related to postoperative consumption and dilution (23). In the vast majority of patients platelet counts will increase thereafter, reaching the presurgery level at about postoperative days 5 to 7. In another study, Miyauchi et al (24) noted that platelet count was reduced markedly with the initiation of bypass and the low level was maintained until the 3<sup>rd</sup> postoperative day. Thrombocytosis following CABG has been described to occur frequently (20–30%) and to be associated with thrombotic complications. Platelet counts returned to normal values within 5 weeks in our study. Postoperative thrombocytosis is a potentially dangerous complication, with an increased risk for postoperative myocardial infarctions, late symptomatic vein graft occlusion (25).

MPV can be useful in predicting the postoperative adverse events in patients undergoing CABG. Khuri et al (26) in their study evaluated that the platelet count fell significantly during CPB, while the MPV decreases significantly after the institution of CPB and reaches its nadir approximately 2 hours later. There is a progressive and significant increase in MPV between 2-72 hours postoperatively, accompanied by a significant rise in platelet mass, suggesting that larger platelets are selectively removed during the CPB. Slavka et al (27) in their study demonstrated that patients with an increased  $\text{MPV} \geq 11 \text{ fL}$  are at higher risk of death due to ischemic heart disease, with hazard ratios comparable to those reported for obesity or smoking. An increased MPV as an indicator of larger, more reactive platelets, resulting from an increased platelet turnover, may represent a risk factor for overall vascular mortality, including myocardial infarction. Platelet volume, and therefore platelet activation, appears to play a causal role in late vein graft disease; hence, MPV may be useful as a post-operative marker of graft success (28).

In our study, the average platelet count decreased gradually to reach the lowest value on day 2 after surgery after which it gradually increased and then gradually decreased to reach normal values on day 21 and preoperative values after three months. The average values of MPV changed

in inverse way according to the average values of platelets (in regenerative bone marrow response).

*Study limitations:* The number of patients is limited. Interesting data could be the difference of this subgroup of patients versus patients undergoing off-pump surgery, which should be a matched and randomized study.

## 5. CONCLUSION

In conclusion, we found that the average values of the three peripheral blood cells parameters, undergo mild to moderate changes after CABG and return gradually to normal and preoperative values after 1-3 months from surgery, when the compensatory function of the bone marrow is preserved and there are no post surgery complications associated with continuous consumption or loss of peripheral blood cellular elements.

Our study shows that in on pump CABG, a stable model of response of the erythrocytes, leukocytes and the platelets happens. Analysis of change over time in the average values of the hematological parameters can be predicted according to the median curve.

**CONFLICTS OF INTEREST: NONE DECLARED.**

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