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

Sotir Lako¹, Teuta Dedej², Tatjana Nurka², Vera Ostreni², Aurel Demiraj³, Roland Xhaxho³, Edvin Prifti³

¹Department of Internal Medicine, American Hospital, Tirana, Albania
²Division of Hematology and Laboratory Medicine, University Hospital Center of Tirana, Albania
³Division of Cardiac Surgery, University Hospital Center of Tirana, Albania

Corresponding author: Edvin Prifti, MD, PhD. Division of Cardiac Surgery, University Hospital Center of Tirana, Rr. Dibra, 370, Tirana, Albania. Tel: + 355682072458. E-mail: edvinprifti@hotmail.com

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) and then gradually increased to reach normal values after one month and the preoperative values after three months. The average platelet count decreased 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) and then gradually increased to reach normal values after one month and the 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 H2O 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 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.
Table 2. Comparison with preoperative values (D-1) ± Standard Deviation (SD), for Red blood cells, Hemoglobin and Hematocrit.

|                | Preoperative RBC± SD, mm³ | Postoperative RBC± SD, mm³ | t   | P         | Preoperative Hg±SD, gr/dl | Postoperative Hg±SD, gr/dl | t   | P         |
|----------------|--------------------------|----------------------------|-----|-----------|---------------------------|---------------------------|-----|-----------|
| D-1;D+2        | 8305.7 ± 59607.9         | 14509.5 ± 4205.9           | 15.7| <0.001    | 13.4 ± 1.6                | 10.4 ± 1.4                | 16.26| <0.001   |
| D-1;D+3        | 8305.7 ± 59607.9         | 11227.7 ± 3720.1           | 8.7 | <0.001    | 13.4 ± 1.6                | 10.7 ± 1.4                | 16.26| <0.001   |
| D-1;D+4        | 8305.7 ± 59607.9         | 36534.8 ± 49011.6          | 15.7| <0.001    | 13.4 ± 1.6                | 10.7 ± 1.4                | 16.26| <0.001   |
| D-1;D+6        | 8305.7 ± 59607.9         | 85063.5 ± 589519.9         | 5.9 | <0.001    | 13.4 ± 1.6                | 11.6 ± 1.6                | 10.2 | <0.001   |
| D-1;D+90       | 8305.7 ± 59607.9         | 4590609.7 ± 596768         | 3.36| <0.001    | 13.4 ± 1.6                | 13.1 ± 1.5                | 1.75 | <0.001   |

Table 3. Comparison with preoperative values (D-1) ± Standard Deviation (SD), for White blood cells, neutrophils, and lymphocytes.

|                | Preoperative RBC± SD, mm³ | Postoperative RBC± SD, mm³ | t   | P         | Preoperative Hg±SD, gr/dl | Postoperative Hg±SD, gr/dl | t   | P         |
|----------------|--------------------------|----------------------------|-----|-----------|---------------------------|---------------------------|-----|-----------|
| D-1;D+2        | 8305.7 ± 59607.9         | 14509.5 ± 4205.9           | 15.7| <0.001    | 13.4 ± 1.6                | 10.4 ± 1.4                | 16.26| <0.001   |
| D-1;D+3        | 8305.7 ± 59607.9         | 11227.7 ± 3720.1           | 8.7 | <0.001    | 13.4 ± 1.6                | 10.7 ± 1.4                | 16.26| <0.001   |
| D-1;D+4        | 8305.7 ± 59607.9         | 36534.8 ± 49011.6          | 15.7| <0.001    | 13.4 ± 1.6                | 10.7 ± 1.4                | 16.26| <0.001   |
| D-1;D+6        | 8305.7 ± 59607.9         | 85063.5 ± 589519.9         | 5.9 | <0.001    | 13.4 ± 1.6                | 11.6 ± 1.6                | 10.2 | <0.001   |
| D-1;D+90       | 8305.7 ± 59607.9         | 4590609.7 ± 596768         | 3.36| <0.001    | 13.4 ± 1.6                | 13.1 ± 1.5                | 1.75 | <0.001   |

3. RESULTS

The mean age of the patients was 61.8 ± 9.0 years (range, 34-82 years). The preoperative demographics and hematological data are presented in Table 1. Time trends of the average values of RBC(mm³), 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) ± 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 of the average values of white blood cells (WBC) (mm³), Neutrophils (mm³), Lymphocytes (mm³) 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)±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 leucocytes 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.
Figure 4. Time trends of percentage values of Red blood cells, White blood cells, Platelets.

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

|                  | Preoperative Platelets±SD, mm$^3$ | Postoperative Platelets±SD, mm$^3$ | 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               | 4.16 | 0.014  |
| D-1;D+90         | 230920.7 ± 65064.7                 | 275154.3 ± 113725.7                | 4.4  | <0.001 | 10.6 ± 1.1              | 10.3 ± 0.9               | 2.7  | 0.007  |

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 anemia 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-
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 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 compensation 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 3rd 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 MPV≥11fL 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 com-
lications 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 plate-
lets 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.

REFERENCES
1. Wang A, Bashore TM. Hematologic Disorders after Cardiac
Surgery. Valvular Heart Disease Book. 2009: 432-35.
2. Papp J, Toth A, Sandor B, Kiss R, Rabai M, Kenyeres P. et al.
The influence of on-pump and off-pump coronary artery by-
pass grafting on hemorheological parameters. Clinical Hemor-
heology and Microcirculation. 2011; 49: 331-346.
3. Beris P, Muñoz M, García-Erce JA, Thomas D, Maniatis A, Van
der Linden P. Perioperative anaemia management: consensus
statement on the role of intravenous iron. Br J Anaesth. 2008
May; 100: 599-604.
4. Kim P, Dixon S, Eisenbrey AB, O’Malley B, Boura J, O’Neill W.
Impact of acute blood loss anemia and red blood cell transfu-
sion on mortality after percutaneous coronary intervention.
Clinical Cardiology. 2007: 30: H35-43.
5. Unal EU, Özen A, Kocabeyoglu S, Durukan AB, Tak
S, Songur M. et al. Mean platelet volume may predict early
clinical outcome after coronary artery bypass grafting. Jour-
nal of Cardiothoracic Surgery. 2013; 16(8): 91.
6. Westenbrink BD, Klein L, de Boer RA, Tijssen JG, Warnica WJ,
Bailot R et al. IMAGINE Investigators. Sustained postopera-
tive anaemia is associated with an impaired outcome after cor-
aray artery bypass graft surgery: insights from the IMAGINE
trial. Heart. 2011 Oct; 97: 1590-1596.
7. van Straten AH, Hamad MA, van Zundert AJ, Martens EJ,
Schönberger JP, de Boer RA, Tijssen JG, Warnica WJ, de
Bailot R et al. IMAGINE Investigators. Sustained postopera-
tive anaemia is associated with an impaired outcome after cor-
aray artery bypass graft surgery: insights from the IMAGINE
trial. Heart. 2011 Oct; 97: 1590-1596.
8. van Straten AH, Hamad MA, van Zundert AJ, Martens EJ,
Schönberger JP, de Boer RA, Tijssen JG, Warnica WJ, de
Bailot R et al. IMAGINE Investigators. Sustained postopera-
tive anaemia is associated with an impaired outcome after cor-
aray artery bypass graft surgery: insights from the IMAGINE
trial. Heart. 2011 Oct; 97: 1590-1596.
9. van Straten AH, Hamad MA, van Zundert AJ, Martens EJ,
Schönberger JP, de Boer RA, Tijssen JG, Warnica WJ, de
Bailot R et al. IMAGINE Investigators. Sustained postopera-
tive anaemia is associated with an impaired outcome after cor-
aray artery bypass graft surgery: insights from the IMAGINE
trial. Heart. 2011 Oct; 97: 1590-1596.
10. van Straten AH, Hamad MA, van Zundert AJ, Martens EJ,
Schönberger JP, de Boer RA, Tijssen JG, Warnica WJ, de
Bailot R et al. IMAGINE Investigators. Sustained postopera-
tive anaemia is associated with an impaired outcome after cor-
aray artery bypass graft surgery: insights from the IMAGINE
trial. Heart. 2011 Oct; 97: 1590-1596.
11. van Straten AH, Hamad MA, van Zundert AJ, Martens EJ,
Schönberger JP, de Boer RA, Tijssen JG, Warnica WJ, de
Bailot R et al. IMAGINE Investigators. Sustained postopera-
tive anaemia is associated with an impaired outcome after cor-
aray artery bypass graft surgery: insights from the IMAGINE
trial. Heart. 2011 Oct; 97: 1590-1596.
12. Ranucci M, Conti D, Castelvecchio S, Menicanti L, Frigiola A,
Ballotta A. et al. Hematocrit on cardiopulmonary bypass and
outcome after coronary surgery in nontransfused patients. Ann
Thorac Surg. 2010 Jan; 89: 11-17.
13. Karkouli K, Wijeyussen DA, Yau TM, McCluskey SA, van
Rensburg A, Beattie WS. The influence of baseline hemoglo-
bin concentration on tolerance of anemia in cardiac surgery.
Transfusion. 2008 Apr; 48: 666-672.
14. Tshaikowsky K, Neddemeyer U, Pscheidl E, von der Emde
J. Changes in circulating blood volume after cardiac surgery
measured by a novel method using hydroxyethyl starch. Clin
Care Med. 2002; 28: 336-341.
15. Santa Ursula Tolosa JA, Criado A, García del Valle S, Pensado
A, Barbolla L, Carmona Aurales JA. Changes in total and dif-
ferential leukocyte counts during heart surgery with extra-
corporeal circulation. Rev Esp Anestesiol Reanim. 1991 Mar;
Apr; 38: 94-97.
16. Abramson, Melton. Leukocytosis basics of clinical assessment.
American Family Physician. 2000: 62: 2053-2066.
17. Kawahito K, Kobayashi E, Ohmori M, Harada K, Kito Y, Fu-
jimura A, et al. Enhanced responsiveness of circulatory neu-
traphils after cardiopulmonary bypass: increased aggrega-
tibility and superoxide producing capacity. Artif Organs. 2000
Jan; 24: 37-42.
18. Gu YJ, Schoen P, Tighchelaar I, Loe LF, BG, Ebelts, Rankin AJ, et
al. Increased neutrophil priming and sensitization before com-
mencing cardiopulmonary bypass in cardiac surgical patients.
Ann Thorac Surg. 2002 Oct; 74: 1173-1179.
19. Asadollahi K, Hastings JM, Beeching NJ, Gill GV, Asadol-
lahi P. Leukocytosis as an Alarming Sign for Mortality in Pa-
tients Hospitalized in General Wards. Iran J Med Sci. 2011
Mar; 36: 45-49.
20. Rashidi F, Jamshidi P, Kheiri M, Asfairazadeh S, Asfairaza-
deh A, Abdolalian F. et al. Is Leukocytosis a Predictor for Re-
currence of Ischemic Events after Coronary Artery Bypass
Graft Surgery? A Cohort Study. ISRN Cardiol. 2012; 2012:
824730.
21. Faraday N, Schunke K, Saleem S, Fu J, Wang B, Zhang J. et
al. Cathepsin G—Dependent Modulation of Platelet Throm-
bus Formation In Vivo by Blood Neutrophils. PLoS One. 2013
Aug 5; 8: e71447.
22. Despotis GJ, Levine V, Goodnough L.T. Relationship between
leukocyte count and patient risk for excessive blood loss after cardiac surgery. Crit Care Med. 1997; 25: 1338-1346.
23. Warkeinten TE, Levine MN, Hirsh J, Horsewood P, Roberts RS,
Gent M. et al. Heparin-induced thrombocytopenia in patients
treated with low-molecular-weight heparin or unfractionated
heparin. N Engl J Med. 1995 May 18; 332: 1330-1335.
24. Miyauchi Y, Isomura K. Quantitative and functional changes
in platelets and their preservation during extracorporeal circu-
lation. The Journal of Cardiovascular Surgery. 1982; 23: 5: 383.
25. Christenson JT, Simonet F, Schmuziger M. Postoperative
Thrombocytosis after Coronary Artery Bypass Grafting: A Poten-
tial Danger even after Hospital Discharge. Medical Princi-
ples and Practice. 1999: 8: 2: 145-155.
26. Kluri SF, Michelson AD, Valeri CR. Effects of cardiopulmo-
nary bypass on hemostasis. No. BUMS-97-03. Boston Univ Ma
SCHOOL OF MEDICINE, 1997.
27. Slava G, Perkmann T, Haslacher H, Greisenegger S, Mar-
sik C, Wagner OF, et al. Mean platelet volume may represent
a predictive parameter for overall vascular mortality and isch-
emic heart disease. Arterioscler Thromb Vasc Biol. 2011 May;
31: 1215-1218.
28. Tavil Y, Sen N, Yazici BU, Hizal F, Açıkgöz SK, Turfan M. et al.
Relationship between elevated platelet volume and saphenous
vein graft disease. Clin Invest Med. 2010 Jun 1; 33: Eh1-167.