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Comparison of Hematological Indices in Patients before and After Coronary Artery Bypass Grafting (CABG)

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ABSTRACT

Subject: Clinically, a reduction in hematocrit (Hct) or hemoglobin (Hb) levels is a notable condition commonly observed in patients undergoing coronary artery bypass grafting (CABG). Postoperative anemia is a risk factor for mortality in patients undergoing CABG, affecting both the early and late stages of recovery. However, the underlying mechanisms remain incompletely elucidated. We aimed to investigate the relation between the hematologic indices with two surgery methods (on-pump & off-pump).

Methods: Fifty consecutive CABG cases were randomly assigned to group I (On-pump, n= 24) and group II (Off-pump, n = 26). General clinical and surgery parameters, hematologic incidence were measured in two blood samples, the first sample was taken from each patient on the morning of the day of surgery after 12-hr fasting, and the second sample on the first postoperative day at 24-hr after surgery. Statistically assessing serum levels pre- and post-CABG and comparing between the two groups was analyzed and the correlation between parameters was evaluated.

Result: In the baseline, there were significant differences between the on-pump and off-pump groups regarding heart rate (HR) (p = 0.002). Investigation after surgery showed that the difference in HR and urea levels in pre- and post-CABG was significant when compared between the two groups. A significant difference was observed in the white blood cell, it became less after the operation. The decrease in platelet and PT level in patients who underwent the on-pump and off-pump surgery (diff = -23.5 and diff = -0.62, respectively) was shown and this difference remained significant between the two groups.

Conclusion: We achieve the on-pump method places greater stress on blood cells, resulting in reduced levels of white blood cell in patient outcomes. It can be suggested that it should be adjusted for patients undergoing both on-pump and off-pump surgeries.

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Introduction

In a significant number of developed and developing countries, coronary artery disease (CAD), largely induced by atherosclerotic in the coronary arteries, is recognized as a major cause of death (1). Managing patients suffering from CAD is challenging due to the complexity inherent in the disease (2). To treat patients suffering from these diseases (regardless of drug treatments) surgical intervention is frequently essential, and in most cases, cardiopulmonary bypass (CPB) is needed. Nonetheless, a range of post-surgical complications including heart failure, multiple organ failure (MOF), respiratory issues, as well as liver and kidney failure can occur (3-5).

Coronary artery bypass grafting (CABG) ranks among the most frequently executed surgical procedures, with around 200,000 operations conducted each year in the United States. In Western Europe, the incidence of CABG is approximately 62 per 200,000 individuals (6). Throughout the past century, the procedure has undergone significant evolution, shifting from a high-risk operation to a relatively secure option (with the current mortality rate ranging between 1% to 2%) (7). Estimates indicate that in Iran, the number of patients requiring CABG each year surpasses ten thousand (8). Even so, the procedure is notably complex and is linked to various complications (7, 9). In this method, the final objective is to bypass a stenosed or occluded coronary artery (9). This surgical approach can be carried out with arterial or venous grafts, with or without cardiopulmonary bypass, and endoscopic harvesting of conduits (10). Conventionally, CABG is executed through the method of cardiopulmonary bypass, known as on-pump CABG. This technique involves halting the heart's function and employing a heart-lung machine to sustain adequate circulation throughout the body (11). Over the last few years, the off-pump CABG method has increasingly become a favored alternative technique in the field of cardiac surgery. Surgeons utilize an artificial circulatory system, known as the heart-lung machine, to replace the functions of the heart and lungs during operations. This strategy involves

bypass grafts on a heart that is actively beating and helps mitigate the inflammatory response typically linked with CPB (12).

Clinically, a decline in hematocrit (Hct) or hemoglobin (Hb) levels is an important condition often observed in patients undergoing CABG (13-15). Studies have demonstrated a relationship between mean platelet volume (MPV) and the occurrence of late saphenous vein graft disease in patients who have undergone CABG (16). A research investigation led by Utku Unal and colleagues demonstrated a significant correlation between preoperative MPV and hematocrit levels, as well as the occurrence of adverse outcomes following CABG. Conversely, the analysis of white blood cell counts, including differential leukocyte counts, revealed no significant correlation with negative events post-CABG (17). Existing literature suggests that an increase in preoperative red blood cell distribution width (RDW) independently forecasts mortality and the occurrence of early complications to CABG (18-21). However, the findings obtained relied on a single preoperative RDW assessment, and there is insufficient information regarding the influence of postoperative changes in RDW (22). According to Urbanowicz et al., neutrophils (among the various postoperative inflammatory indices) emerge as one of the most significant predictors of long-term survival after off-pump coronary artery bypass surgery, especially when evaluated in conjunction with preoperative characteristics (23). Despite various research, there is still limited information available about the levels of hematological parameters before and after surgery. Therefore, the upcoming study aims to investigate blood parameters in patients before and after CABG.

Patients and Methods

Patients

This study was conducted at the Imam Reza Hospital in Mashhad, specifically in the Department of Cardiac Surgery. Fifty patients aged between 40 and 80 years, who sought coronary artery bypass surgery and provided written consent, were consecutively enrolled. The study received ethical approval from the Mashhad University of Medical Sciences (IR.MUMS.IRH.REC.1403.065) and informed consent was obtained from all participants. The selection criteria for CABG surgery were based on guidelines from the American College of Cardiology/American Heart Association Task Force on Practice Guidelines, focusing on patients with stable angina pectoris. Two groups of patients were created, on-pump or off-pump groups according to surgical technique that was determined by the cardiac surgeon. Of 50 patients, twenty-four patients in the group underwent CABG using the on-pump technique, while twenty-six patients had the off-pump approach. Patients typically take medications such as Osivix, Plavix, and ASA. They were instructed to discontinue these medications five days prior to the operation. Additionally, some patients with high blood pressure were prescribed drugs like Metoprolol, Inderal, Losartan, Captopril, Nitroglycerin, and Nitrocantin.

Inclusion and Exclusion of Criteria

Patients (aged between 40 and 80 years), who refer to the Imam Reza Hospital in Mashhad and undergoes CABG were consecutively enrolled. The following criteria excluded patients from participating in the study: 1) those without written consent, 2) patients with an EF < 20%, 3) individuals with preoperative kidney disease indicated by a serum creatinine > 0.3 mg/dL, 4) patients with coagulation disorders prior to surgery, 5) individuals with concurrent valve and coronary diseases, 6) The need to perform unanticipated complex surgery during the operation, 8) Death of the patient in the operating room, Flow diagram of the study of the study was shown in Figure 1.

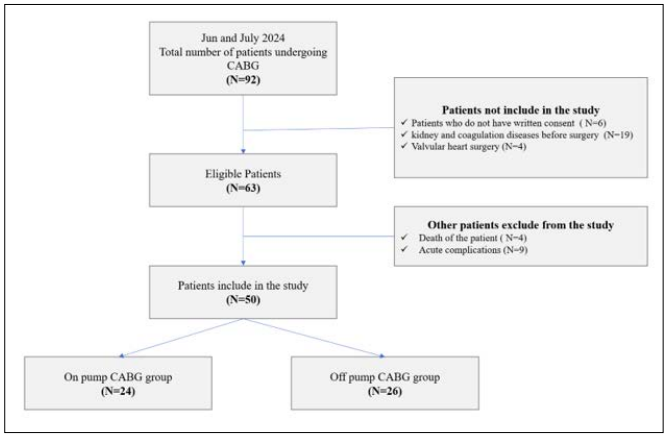

Figure 1: Flow diagram of the Study.

Measurements

Upon patient enrollment, essential demographic information is collected: age (in years) and sex. A unique case number is assigned for the surgery and the operation date is recorded. The type of vascular disease is categorized as either 1VD (single-vessel disease), 2VD (two-vessel disease), 3VD (three-vessel disease), or LM (left main coronary artery disease). Additionally, the Ejection Fraction (EF, %) is measured to assess left ventricular function. Pre-existing cardiovascular risk factors are then evaluated. 1) Hypertension is defined as systolic blood pressure (SBP) ≥ 140 mmHg, diastolic blood pressure (DBP) ≥ 90 mmHg, or the current use of antihypertensive medications. 2) diabetes mellitus (DM), based on a fasting blood sugar level of ≥ 126 mg/dL, or if the patient is currently taking diabetic medications. 3) Chronic conditions like chronic renal failure (CRF), 4) chronic obstructive pulmonary disease (COPD) is screened for, with their presence or absence recorded. 5) dyslipidemia is assessed based on total cholesterol ≥ 200 mg/dL, LDL-C ≥ 130 mg/dL, or the current use of cholesterol-lowering medications.

Intraoperative and Postoperative Monitoring

Upon ICU admission, meticulous monitoring commences to identify and address potential postoperative complications. Blood loss is recorded at specific time points: 1, 6-, 12-, 24-, and 48-hours following surgery. The occurrence of atrial fibrillation (AF) and ventricular arrhythmias (VT/VF), is tracked. Additionally, any reoperations or blood transfusions required are documented.

The Vasopressor-Inotropic Score (VIS) is calculated as follows: Vasopressor-Inotropic score = ([Dopamine + Dobutamine] ×1) + (Milrinone ×15) + ([Epinephrine + Norepinephrine + Isoproterenol] ×100), and is recorded upon ICU admission and at regular intervals throughout their stay (6-, 12-, 24-, and 48-hours post-admission) to assess their hemodynamic stability. Hemodynamic parameters (systolic, diastolic, and mean arterial pressures (MAP) along with heart rate (HR) are continuously monitored and recorded at the same intervals as the VIS.

Arterial blood gas measurements are taken pre-CPB, every 30 minutes during CPB, immediately upon ICU admission, and again at 12- and 24-hours post-admission. CPB parameters are documented, including aortic cross-clamp time and total CPB duration. Additionally, inotropic support needs within the first 2 hours after surgery and the use of an intra-aortic balloon pump (IABP) are recorded. Mortality rates are tracked during hospitalization and up to one month after discharge. Surgical site infections (SSIs), categorized as superficial or deep (with potential dehiscence), are monitored. The duration of mechanical ventilation and length of stay in both the ICU and the hospital are

documented. We note any difficulties encountered during extubating (weaning process) within 48 hours post-surgery. Neurological complications, if any, are recorded. Blood samples are drawn to measure serum glucose and liver enzyme levels preoperatively, upon ICU admission, and 24 hours later.

Statistical Analysis

The patients' information was collected, sorted and processed and then entered into SPSS version 20 software. The description of the data was expressed with the help of descriptive statistics indicators in the form of frequency and mean + standard deviation and in the form of suitable tables and graphs. After checking the normality of the data, T-test or Mann-Whitney-U was used to check the relationship between the qualitative and quantitative variables, and the relationship between the qualitative variables was performed using the chi-square test. Also, in order to control intervening variables, logistic regression model was used to determine the relationship between the independent variable and the categorized values of the dependent variables. A statistically significant level of 5% was considered.

Result

Baseline Characteristics of Patients

The findings from the initial analysis revealed the baseline characteristics of the patients presented in Table 1. Among the 50 patients, there were 15 females (30%) and 35 males (70%). The average age was 59.92 ± 10.71 years. The subjects were divided into two groups: On-pump (N=24) and Off-pump (N=26). The distribution of men and women was balanced in both groups. Significant differences were observed between the on-pump and off-pump groups regarding heart rate, with means of 90.63 ± 20.64 and 74.42 ± 14.06, respectively (p = 0.002). However, no notable differences were found in other variables between the two groups. There were not significant differences between the on-pump and off-pump groups in terms of cross clamp and CPB and postoperative mechanical ventilation duration.

Table 1: Characteristics of Patients Undergoing Coronary Artery Bypass Surgery (CABG) and Comparing it in Two Methods, on Pump and Off Pump.

Variable	On pump, N=24	Off pump, N=26	P-value
Characteristics			
Age	58.67±11.93	61.08±9.6	0.4
Female	7(29.2)	8(30.8)	0.9
Male	17(70.8)	18(69.2)	
CVD Type			
1VD	-		0.6
2VD	5(20.8)	7(26.9)	
3VD	14(58.3)	16(61.5)	
4VD	5(20.8)	3(11.5)	
Discerption of Operation			
ICU Duration	2.96±2.17	2.50±0.99	0.35
SBP	111.38±15.03	111.31±17.62	0.98
DBP	64.83±12.23	62.42±10.67	0.46
Heart Rate	90.63±20.64	74.42±14.06	0.002
EF %	46.2±9.5	49.3±11.4	0.3
Cross Clamp Duration (min)	49.27±17.83	-	-
CPB Duration (min)	73.04±20.84	-	-
Duration of Mechanical Ventilation (hours)	9.42±3.3	9.65±5.4	0.8

Comparing pre- and Post-CABG

The evaluation of hematological incidence before and after coronary artery bypass grafting (CABG) are displayed in Table 2. This table presents the baseline parameter levels and their differences (labeled as "diff") 24 hours after surgery, along with the statistically significant variations observed. As indicated, there was a significant difference in MCHC levels before and after the operation in patients who underwent on-pump surgery. In this group, a significant decrease was observed in platelet and PT (-23.5±41.14 and -0.62±1.15, respectively). However, patients who underwent off-pump surgery showed an increase in PT.

As can be seen from the result of white blood cell indices, a significant difference was observed in the serum levels of WBCs and lymphocytes after surgery in both groups. What is interesting in this data is that decrease difference in lymphocytes level in on-pump group was two-fold more than off-pump (-8.2±15, -4.8±5.58, respectively).

Data are shown as Mean ± SD for Normal Variables and Median (Interquartile Range) for Non-Normal Variables. Abbreviations:

Table 2: Comparing the Hematology Markers in Patients before and after CABG and Comparing it in two Methods, on Pump and Off Pump.

	On pump (N=24)			Off pump (N=26)			
Variable	**Baseline**	**Diff**	**P-value**	**Baseline**	**Diff**	**P-value**	***P value**
White Blood Cell Indices							
WBCs (103/M)	15.15±6.4	-2.55±4.3	0.008	13.84±4.5	-2.01±4.2	0.025	0.001
Lymphocytes	14.02±14.9	-8.2±15	0.015	13.9±4.3	-4.8±5.58	0.001	0.94
Neutrophils	81.22±2.63	7.8±1.2	0.06	89.25±3.6	12.3±3.2	0.2	0.154
INR	1.19±1.21	-0.2±0.19	0.615	1.6±2.25	-0.49±2.2	0.280	0.814
RED Blood Cell Indices							
RBC (103/M)	3.86±0.71	-0.23±0.62	0.085	4.02±0.46	-0.009±0.55	0.931	0.153
Hgb (g/dL)	10.97±1.7	-0.49±1.76	0.1	11.5±1.8	-0.34±3.3	0.903	0.394
Hct (%)	10.97±4.73	-2.02±4.8	0.054	34.2±4.6	-0.107±4.7	0.908	0.005
MCV (fL)	85.02±5.5	-0.62±1.5	0.062	84.8±4.3	-0.046±2.003	0.907	0.001
MCH (pg)	28.59±2.1	0.28±0.9	0.147	28.6±2.1	0.39±1.17	0.099	0.001
MCHC (g/dL)	28.59±2.1	0.6±1.1	0.018	33.6±1.4	0.51±1.5	0.106	0.011
RDW (%)	10.87±3.53	-2.02±0.2	0.153	11.45±2.53	-1.02±2.5	0.210	0.59
Platelet indices							
Platelet (103/uL)	194.2±53.7	-23.5±41.14	0.01	241.3±75.9	-13.42±44.47	0.136	0.001
MPV (fL)	10.19±1.21	-0.2±0.19	0.615	9.6±0.25	-0.49±2.2	0.280	0.410
PDW (fL)	45.39±7.56	1.2±0.18	0.525	49.5±2.25	2.48±3.8	0.580	0.851
PT	14.9±1.4	-0.62±1.15	0.015	13.83±1.5	4.3±25.01	0.389	0.002
PTT	38.75±4.3	-4.65±4.03	0.220	38.50±6.1	-4.6±5.1	0.168	0.562

* P value of difference between diff in two group. The P-value less than 0.05 was considered statistically significant. Data are shown as Mean ± SD for normal variables and Median (Interquartile Range) for non-normal variables.
Abbreviations:
WBC: White Blood Cell; MID: Mid-Range Absolute Count; RBC: Red Blood Cell; HGB: Hemoglobin; HCT: Hematocrit;
MCV: Mean Cell Volume; MCH: Mean Cell Hemoglobin; MCHC: Mean Cell Hemoglobin Concentration ; RDW: Red Blood Cell **Distribution Width; MPV:** Mean Platelet Volume; PDW: Platelet Distribution Width.
T Student and Mann whitney Tests were used for Analysis. P-value < 0.05 is Considered Statistically Significant.

Comparing on-Pump and Off-Pump CABG
Table 2 illustrated the comparison of parameters levels between the on-pump and off-pump methods, before and after CABG. The last column in the table indicates the p-value for the variance between "diff" in the on-pump and off-pump groups.

Comparison of the changes of WBC as post- minus pre-operation data between on- and off-pump CABG surgery was demonstrated that there were decreasing changes in group 1 and group 2. These differences were significant in both groups and also P value of difference between diff in WBC in studied groups was remained significant (P=0.001).

In addition, P value of difference between diff in MCV, MCH, MCHC, and Hct in studied groups was remained significant. As can be seen from the table, A significant decrease was observed in the levels of Platelet (-23.5±41.14) and PT (-0.62±1.15) in on pump group. Also, P value of difference between diff in these parameters in studied groups was remained significant.

Discussion
A systematic evaluation of peripheral blood hematologic parameters following cardiac surgery is essential for monitoring changes and implementing necessary corrections. Anemia is a common condition characterized by a deficiency of red blood cells or hemoglobin in the blood, leading to decreased oxygen transport to tissues (24). Its prevalence varies based on the population and underlying health conditions. In the context of patients undergoing CABG (coronary artery bypass grafting), studies have shown that anemia can be observed in over 90% of cases, highlighting its significant impact on this patient group (25). This can be attributed to acute blood loss occurring during and after surgery. Approximately 85% of intraoperative and early postoperative bleeding is related to technical factors and is caused by CPB, which leads to hemodilution.

As mentioned in the literature review, postoperative anemia is a risk factor for mortality in patients undergoing CABG, both in the early and late stages (26). According to the primary objective of this project, we have monitored changes in hematologic incidence throughout the operation to gain a deeper understanding of anemia before and after the CABG intervention. Blood loss is a frequent issue in cardiac surgery, often necessitating additional interventions, particularly in the case of significant blood loss (27). One of the important issues that emerges from our findings that was not investigated in other studies, is decreasing the level of WBC after 24 hours operation in patients who underwent surgery with on-pump method is more reduced than in patients who were operated

with off-pump method significantly. A possible explanation for this might be that high WBC count prior to CABG surgery serves as an independent risk factor for ischemic events occurring one year following the surgery (28). Despotis et al. (22) indicated that patients exhibiting the highest increase in white blood cell (WBC) count during cardiopulmonary bypass (CPB) are most prone to bleeding in the first 24 hours post-surgery. On-site WBC count measurements can act as an indicator of the inflammatory response to CPB, aiding in the identification of patients who are at an elevated risk for significant bleeding. With this insight, physicians may be able to apply anti-inflammatory medications and blood conservation strategies to manage the situation (29).

Our study was demonstrating a significant difference in lymphocytes and neutrophil in both group of patients who underwent the on-pump and off-pump surgery. It is encouraging to compare our investigation with that found by point out the hematological changes in patients undergoing coronary artery bypass surgery. They showed the average levels of leukocytes and neutrophils rose quickly, reaching their peak on day 2, whereas the average lymphocyte count dropped sharply, reaching its lowest point on day 1 after surgery (+74.7%, +127.1%, and -52.4% respectively compared to preoperative values, $p<0.001$) (30).

Prior studies have not noted the importance of difference between kind of CABG surgery. We found that a significant decrease was observed in the levels of Platelet and PT in on pump group and these parameters in studied groups was remained significant. Lako (2015) showed that the average platelet count decreased to the lowest value on day 2 after surgery from the preoperative (30). The acute decrease in hematocrit (Hct) led to a reversible impairment of platelet function, which was evident by an increase in bleeding time (BT) and a reduction in the Thromboxane B2 level in shed blood at the template BT site (31). In most patients, platelet counts typically rise thereafter, returning to pre-surgery levels around postoperative days 5 to 7 (32). Miyauchi et al. observed a significant decrease in platelet count upon the start of bypass, with this low level persisting until the third postoperative day (33).

Conclusion

Our findings showed that decreasing the level of WBC after 24 hours operation in patients who underwent surgery with on-pump method is more reduced than in patients who were operated with off-pump method significantly. The average values of leukocytes in pre and post operation increased, while this difference was not significant between on- and off- pump. We found that a significant decrease was observed in the levels of Platelet and PT in on pump group and these parameters in studied groups was remained significant.

Declaration Section

Informed Consent

Informed consent was obtained from all individual participants included in the study.

Authors' Contributions

All authors were involved in the interpretation of the data and contributed to writing the manuscript. All authors read and approved the final manuscript.

Availability of Data And Materials

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethics Approval

The approval of the ethics committee of the Mashhad University of Medical Sciences (IR.MUMS.IRH.REC.1403.065) was received and informed consent form.

Consent for publication

Not applicable.

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None.

Conflict of Interest

The authors have no conflict of interest to disclose

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