The role of immature platelet count and immature platelet fraction in determining the need for transfusion in patients undergoing CABG

cihan yücel[1], Serkan Ketenciler[1], and Nihan Kayalar[1]

[1]Okmeydani Training and Research Hospital

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Abstract

Objective: Platelet dysfunction has been shown to play a role in postoperative bleeding; however, it is not clear whether immature platelets (IP) can induce appropriate homeostasis to prevent excessive bleeding in patients undergoing CABG. This study investigated IP count (IPC), IP fraction (IPF) and mean platelet volume (MPV) throughout the hospitalization of patients undergoing CABG to elucidate their impact on postoperative bleeding and need for transfusion. Methods: Fifty consecutive patients undergoing elective CABG were included in this prospective study. All CABGs were performed by the same surgical team in a standardized fashion utilizing on-pump technique. IP and IPF were measured preoperatively, after the completion of surgery and at postoperative 1st,3rd, and 5th days. Whether need for transfusion was associated with IP, IPF, MPV and platelet count was the primary outcome measure of this study. Results: A significant increase in IPC and IPF was observed at the postoperative first day compared to baseline values. Preoperative IP and IPF were negatively correlated with intraoperative blood transfusion ($p=0.017$, and $p=0.049$, respectively). Duration of the operation, and preoperative hemoglobin and hematocrit levels were significantly correlated with the length of hospital stay. However, neither IP nor IPF were associated with the total amount of blood components used throughout the hospitalization, and they were also unassociated with the length of hospital stay. Conclusion: Although IPC and IPF are weakly correlated with postoperative drainage and blood transfusion frequency, they appear to have very little use –if any– in the prediction of postoperative bleeding in patients undergoing CABG

INTRODUCTION

The coronary artery bypass graft (CABG) procedure is among the most common cardiac surgical procedures.[1,2] It has become the final treatment to reduce symptoms and mortality in subjects with ischemic heart disease resulting from multivessel coronary artery disease (CAD) or left-main disease for >40 years.[3] Older age, female gender, the presence of obesity, diabetes, hypertension, chronic obstructive pulmonary disease, extra-cardiac arteriopathy, neurologic dysfunction, left-main stem disease, renal dysfunction, reduced left ventricular ejection fraction, and the development of perioperative myocardial infarction and atrial fibrillation are among the factors shown to increase in-hospital mortality in patients undergoing CABG.[4]

Excessive bleeding is another important risk factor for in-hospital mortality after CABG. Consumption of coagulation factors, and impaired platelet function are responsible for about half of the postoperative bleeds and re-explorations following CABG.[5] In addition to an increase in in-hospital mortality, the need for blood transfusions as a result of excessive bleeding prolongs hospital stay and increases healthcare costs.

The number of immature platelets (IP) and immature platelet fraction (IPF) may provide clues concerning the status of platelet function. Immature platelets are young cells that have recently been released into the circulation, and are considered indicators of bone marrow recovery.[6] The IP count (IPC) and IPF values may be used as a representation of the number of recently produced platelets released into the circulation by regenerated BM megakaryocytes, thereby reflecting the level of thrombopoiesis.[7] Platelet dysfunction has been shown to play a role in postoperative bleeding; however, there is very little data pertaining to the role of these immature thrombocytes in the induction of sufficient homeostasis and the prevention of excessive bleeding following CABG.

The purpose of this study was to investigate IPC, IPF and mean platelet volume (MPV) values throughout the hospitalization of patients undergoing CABG in order to elucidate whether they were associated with postoperative bleeding and the need for transfusion.

MATERIALS AND METHODS

Study group

Fifty consecutive patients undergoing elective CABG in the Okmeydanı Training and Research Hospital were included in this prospective study. Subjects with a history of bleeding diathesis or abnormal preoperative coagulation test results (international normalized ratio [?] 1.3, activated partial thromboplastin time >40 s) and those with chronic liver disease were excluded. Subjects scheduled for re-operation, and those in whom postoperative hemodynamic support with intraaortic balloon pump (IABP) or extracorporeal membrane oxygenation (ECMO) were required, were also excluded. Written informed consent was obtained from all participants. The study was approved by the institutional review board and was conducted in accordance with the Helsinki declaration (No:48670771-514.10).

Surgical Technique

All CABG procedures were performed by the same surgical team in a standardized fashion utilizing an on-pump technique. Arterial and venous catheters were inserted into the radial artery and right jugular vein before sternotomy. Blood pressure, central venous pressure, urine output and oxygenation were monitored throughout the surgery. All patients underwent standard median sternotomy under general anesthesia. Grafts were prepared after heparinization (300 IU/kg). After placement of the Favalaro retractor, LIMAs were harvested in the form of pedunculated grafts in all patients by the use of electrocautery and hemoclips. During and after harvesting of LIMAs, a warm papaverine solution was used to prevent LIMA spasm. Following the performance of side-to-side LIMA and SVG anastomosis, coronary flow in the distal LAD was checked and side-to-end LIMA-LAD artery anastomosis was carried out using 8-0 prolene sutures. Saphenous Vein Grafts (SVGs) were harvested endoscopically and were grafted to the coronary arteries by employing the end-to-side anastomotic technique. An epicardial pacing wire was then positioned on the anterior cardiac surface and mediastinal and thoracic cannulas were placed for drainage. The sternum was closed by surgical steel wires as a complete layer. 4-0 vicryl was used for skin and subcuticular closure. Following the operation, patients were transferred to the intensive care unit (ICU) and received enoxaparin 0.1 mg/kg twice daily for three days. From the first postoperative day, all patients received a lifelong daily maintenance dose of 100 mg of aspirin.

Coagulation tests

Complete blood count, Prothrombin Time (PT/INR), Partial Thromboplastin Time (PTT) and fibrinogen level were measured at baseline (preoperatively), following the completion of the surgery and at postoperative 1^{st}, and 3^{rd} days and before discharge. The IPC and IPF were also measured preoperatively, following the completion of the surgery and at postoperative 1^{st}, 3^{rd}, and 5^{th}days. EDTA-anticoagulated whole-blood samples were used to measure the platelet count and percentage of IPF (IPF%) using a Sysmex XN-9000 analyzer (Sysmex, Kobe, Japan).[8]

Primary endpoint

Demographic data, details of the surgical procedure, operation time, aortic cross-clamp time, coagulation test results, mean platelet volume, platelet count, IPC and IPF, erythrocyte and whole blood transfusions, and length of hospital stay were recorded. The association between need for transfusion and the values of IPC, IPF, MPV and platelet count was the primary outcome measure of this study.

Statistical analysis

All analyses were performed on SPSS v21 (SPSS Inc., Chicago, IL, USA). For the normality check, the Kolmogorov-Smirnov test was used. Data are given as mean ± standard deviation or median (1st quartile - 3rd quartile) for continuous variables according to normality of distribution, and as frequency (percentage) for categorical variables. Repeated measurements were analyzed with the Friedman's analysis of variances by ranks since parametric test assumptions were not met. Post-hoc pairwise comparisons were performed with the Bonferroni correction method. Multiple linear regression analysis (stepwise selection method) was performed to determine significant factors associated with outcomes. $p<0.05$ values were accepted as statistically significant results.

RESULTS

Fifty patients meeting the inclusion criteria were enrolled in the study (mean age 63.08 ± 10.77 years, 78% male). Demographic features and patients characteristics are listed in **Table 1** . Mean duration of operation was 290.70 ± 53.02 minutes and median aortic cross clamp time was 65.5 (56 - 76) minutes. Median intraoperative UF heparin dose was 45 (45 - 50) x 10^3 units. Overall, 38% of the subjects had received erythrocyte suspension and 18% had received fresh frozen plasma during the operation. Postoperative drainage volumes at the 2^{nd}, 4^{th}, 6^{th}, 12^{th}, and 24^{th} hours were 100 (50 - 200) mL, 200 (150 - 300) mL, 300 (200 - 400) mL, 450 (350 - 550) mL, and 525 (400 - 700) mL, respectively. With regard to the distribution of postoperative transfusions, it was found that 26% of the study subjects received 1 unit of erythrocyte suspension, 26% received 2 units of erythrocyte suspension, and 10 % received 3 units of erythrocyte suspension. For fresh frozen plasma, the distributions were: 1 unit in 12%, 2 units in 28%, and 3 units in 14% of the study subjects. Median length of hospital stay was 6 (6 - 8) days. In-hospital mortality occurred in 2% of the patients **(Table 2)** .

The change in blood test results throughout the hospitalization are presented in **Table 3.** A significant increase in IPC and IPF values was observed at the postoperative first day compared to baseline values. Preoperative IPC and IPF were negatively correlated with intraoperative blood transfusion ($p=0.017$, and $p=0.049$, respectively). Duration of the operation, preoperative hemoglobin and hematocrit levels were significantly correlated with the length of hospital stay**(Table 4)** .

Multiple linear regression analysis was performed to determine significant associates of the amount of blood components used. We found that longer duration of operation ($p=0.002$) and higher preoperative MPV values ($p=0.031$) were associated with higher numbers of blood components used **(Table 5)** . Other variables included in the model, age ($p=0.099$), gender ($p=0.245$), surgery ($p=0.859$), aortic cross-clamp duration ($p=0.744$), intraoperative heparin ($p=0.538$), preoperative red blood cell count ($p=0.268$), preoperative hemoglobin ($p=0.162$), preoperative hematocrit ($p=0.295$), preoperative platelet ($p=0.936$), preoperative IPF ($p=0.376$), preoperative IPC ($p=0.315$) and preoperative INR ($p=0.903$) were found to be non-significant.

DISCUSSION

We hypothesized that IPC and IPF would have an impact on intra- and postoperative bleeding in patients with CABG, and thus, these parameters would be associated with the number or volume of transfusions. Our findings showed that IPC and IPF were negatively correlated with the amount of blood components transfused intraoperatively, albeit weakly. Preoperative IPC was also found to be weakly correlated with postoperative drainage at the 12^{th} hour. However, neither IPC nor IPF were associated with the total amount of blood components used throughout hospitalization, and they also had no relationship with the length of hospital stay.

Parallel to the increase in technical advances and number of the angiographies performed to diagnose the presence of the coronary artery disease, the number of the patients scheduled for CABG has increased in recent years.[9,10] The CABG procedure is currently the standard of care for treatment of multivessel coronary artery disease, particularly in subjects with concomitant diabetes and left ventricular systolic dysfunction.[11-13] However, it still has an in-hospital mortality rate of about 3% and it has been established that intra-and postoperative bleeding events account for a considerable portion of the mortality associated with CABG procedures .[14]

Several factors, including reduced coagulation factors and a low platelet count may lead to coagulopathy following CABG. Previous data have shown that platelet counts after CABG are independent predictors of excessive blood loss.[15] A prolonged closure time, which indicates platelet dysfunction, has been shown to predict blood product transfusion in children undergoing cardiac surgery.[16] Studies utilizing multiple electrode impedance aggregometry (MEIA) and light transmission aggregometry (LTA) demonstrated significant platelet dysfunction after CABG, with partial recovery within 24 hours after surgery .[17]

Immature platelet count and IPF, which represent the young cells that have recently been released into the circulation, are considered to be associated with platelet function. These young platelets have a greater number of granules and higher volume than the older ones, and thus, may be more effective in facilitating homeostasis in case of bleeding.[7] Although platelet count and platelet dysfunction measured by different techniques have been shown to precipitate excessive bleeding after CABG, there is currently no data concerning the impact of IPC and IPF on postoperative bleeding in patients undergoing CABG.[18-20] Our study is the first to demonstrate real-life data regarding the association of IPC and IPF with postoperative drainage and need for transfusion in patients who had undergone CABG. We found that IPF increases shortly after CABG compared to preoperative values, however, IPC returns to baseline values on the 5^{th} postoperative day. Our findings show that preoperative IPF has a weak correlation with the amount of blood components transfused intraoperatively. Nonetheless, IPF has no significant association with the total amount of the blood components used throughout hospitalization and the length of the hospital stay. These findings show that IPF has limited value to predict postoperative drainage and the need for postoperative blood transfusion.

Conclusion

In conclusion, IPC and IPF have weak correlations with postoperative drainage volumes and the need for blood transfusion. They appear to have little value –if any– in the prediction of postoperative bleeding in patients undergoing CABG. Further research with larger sample size may be required to understand the role of IPs in coagulopathy after surgical procedures, and studies with a prospective design that stratify patients based on various other characteristics may aid the search for other parameters (especially blood indices) that could be utilized to predict excessive bleeding in this patient population.

Conflict of Interest

No potential conflicts of interest relevant to this article are reported.

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Table legends:

Table 1. Summary of patients' characteristics

Table 2. Summary of intraoperative and postoperative characteristics

Table 3. Summary of laboratory measurements

Table 4. Correlations between variables

Table 5. Significant factors of the numbers of blood components used, multiple linear regression analysis

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