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Association Between Prolonged Closure Time on the Platelet Function Analyzer-200 and Risk of Perioperative Blood Transfusion

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Dear Editor,

Platelet Function Analyzer (PFA)-100 (Siemens, Erlangen, Germany) has been proposed for preoperative screening because it is simple, easy-to-use, and can evaluate both the adhesion and aggregation of platelets [1]. Recently, PFA-100 has been upgraded to PFA-200, but the principle and method are the same. Previous studies reported conflicting opinions on the association of PFA-100 (Siemens) with blood transfusion, but diseases and surgery types differed across studies [1-4]. Therefore, we examined the association between PFA-200 results and the frequency of perioperative blood transfusion across surgery types.

We retrospectively analyzed the results of PFA-200 and other laboratory tests such as complete blood count (CBC), prothrombin time (PT), and activated partial thromboplastin time (aPTT) as well as transfusion records, medication history, and surgery types from 2,474 patients who underwent surgery with preoperative PFA-200 screening between January and December 2014. We excluded 477 patients with low hematocrit (<35%) or platelet counts ($<150.0\times10^9$/L), as well as seven infants under one year old [5, 6]; thus, the final study group comprised 1,990 patients (Table 1). Surgery types were classified as major operations (e.g., gastrectomy, total hip arthroplasty, and cholecystectomy) and minor operations (e.g., tonsillectomy, percutaneous vertebroplasty, and tracheostomy). The study was approved by the Hallym University Sacred Heart Hospital Institutional Review Board (No. 2017-I045).

The PFA-200 system consists of a reservoir, capillary, and cartridges containing collagen/epinephrine (CEPI) or collagen/adenosine diphosphate (CADP). Platelets in the blood are activated by CEPI or CADP, adhere, and aggregate to form a plug that gradually obstructs the capillary hole in the cartridge. The closure time (CT), measured in seconds, represents platelet function [7]. The reference ranges in our laboratory were 80–191 seconds and 62–119 seconds for CEPI and CADP, respectively. We categorized patients as "prolonged CT" if CEPI-CT or CADP-CT was longer than the reference ranges and as "normal CT" if both were within the reference ranges.

The statistical analysis was performed using SPSS Statistics for Windows, version 24 (IBM Corp., Armonk, NY, USA). The Mann–Whitney U test was used to compare continuous variables. The chi-square test or Fisher's exact test was used to compare the frequency of blood transfusion between groups. The association between prolonged CT and the frequency of blood transfusion was evaluated using logistic regression. $P<0.05$ was con-

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Table 1. Clinical and laboratory characteristics of the study patients according to the PFA-200 results

	Normal CT group (N=1,645)	Prolonged CT group (N=345)	*P**
Age (yr)	45 (24–56)	50 (34–62)	<0.001
Male:Female	54.5:45.8	50.1:49.9	0.172
Blood type O:non-O	23.2:76.8	40.0:60.0	<0.001
Major:minor operation	65.5:34.5	63.2:36.8	0.419
Medication (-):medication (+)†	97.9:2.1	97.4:2.6	0.581
CEPI-CT (sec)	119.0 (102.0–140.0)	227.0 (196.0–250.0)	<0.001
CADP-CT (sec)	83.0 (72.0–94.0)	110.0 (88.0–129.0)	<0.001
PT (sec)	13.0 (12.6–13.5)	13.1 (12.6–13.6)	0.304
aPTT (sec)	36.0 (33.5–39.2)	36.5 (33.9–39.4)	0.141
RBC count ($\times 10^{12}$/L)	4.69 (4.35–5.00)	4.61 (4.25–4.93)	0.007
Hct (%)	41.1 (38.7–44.4)	40.6 (37.9–43.8)	0.014
Hb (g/L)	141 (132–153)	140 (130–152)	0.072
MCV (fL)	89.3 (86.1–92.2)	89.5 (85.8–92.6)	0.540
MCH (pg)	30.70 (29.40–31.7)	30.70 (29.70–31.90)	0.157
MCHC (g/L)	343 (337–349)	344 (338–351)	0.099
RDW (%)	12.5 (12.2–12.9)	12.6 (12.2–13.0)	0.025
WBC count ($\times 10^9$/L)	7.0 (5.7–8.8)	6.90 (5.6–8.6)	0.839
Platelet count ($\times 10^9$/L)	256.2 (226.0–303.0)	248.0 (208.0–300.0)	<0.001
MPV (fL)	7.6 (7.1–8.6)	7.8 (7.3–9.0)	0.001

Values are presented as median (interquartile range) or percentages.
*Mann–Whitney U test, chi-square test, or Fisher's exact test was used to compare the two groups; †Antiplatelet agent or anticoagulant.
Abbreviations: PFA-200, Platelet Function Analyzer-200; CT, closure time; CEPI, collagen/epinephrine; CADP, collagen/ADP; PT, prothrombin time; aPTT, activated partial thromboplastin time; RBC, red blood cell; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; RDW, red cell distribution width; WBC, white blood cell; MPV, mean platelet volume.

Table 2. Perioperative blood transfusion frequency according to the PFA-200 results

	N	Transfusion (+) (N=67)	Transfusion (-) (N=1,923)	*P**†	Odds ratio† (95% CI)
Normal CT group	1,645	47 (2.9)	1,598 (97.1)		
Prolonged CT group	345	20 (5.8)	325 (94.2)	0.013	2.09 (1.22–3.58)
CEPI only	205	10 (4.9)	195 (95.1)	0.130	1.74 (0.87–3.50)
CADP only	72	4 (5.6)	68 (94.4)	0.162	2.00 (0.70–5.71)
CEPI and CADP	68	6 (8.8)	62 (91.2)	0.016	3.29 (1.36–7.99)

Values are presented as N (%).
*Chi-square test or Fisher's exact test was used to compare the proportion of transfused patients between each prolonged CT group and normal CT group; †Compared with the normal CT group.
Abbreviations: PFA-200, Platelet Function Analyzer-200; CI, confidence interval; CT, closure time; CEPI, collagen/epinephrine; CADP, collagen/ADP.

sidered statistically significant.

Table 2 shows the breakdown of patients by CT and blood transfusion frequency. Sixty-seven patients (3.4%) received transfusion on the day of surgery. All patients received RBCs; additionally, 12 patients were transfused with fresh frozen plasma (FFP); one with FFP and platelet concentrates; and one with FFP, platelet concentrates, and cryoprecipitate. The proportion of transfused patients was higher in the prolonged CT group than in the normal CT group (2.9% vs 5.8%, $P=0.013$, odd ratio: 2.09, 95% confidence interval [CI]: 1.22–3.58). Logistic regression indicated that prolonged CT was associated with the risk of transfusion (odds ratio: 2.09, 95% CI: 1.36–7.99). Furthermore, patients with prolonged CEPI-CT and CADP-CT showed a much higher proportion of transfusion than in patients with normal CT (2.9% vs 8.8%, $P=0.016$) and risk of transfusion (odds ratio: 3.29, 95% CI: 1.36–7.99).

We also analyzed the association between prolonged CT and proportion of transfused patients who had taken only antiplatelet agent or anticoagulant (N=44), to exclude the effect of medication on this association. In these patients, the prolonged CT group showed a higher proportion of transfused patients than the normal CT group (5.7% vs 33.3%, $P=0.05$).

Previous studies have reported conflicting findings regarding the association of prolonged CT on PFA-100 with perioperative blood transfusion. Sucker *et al.* [5] showed that RBC transfusion is strongly associated with prolonged CT during aortic valve replacement surgery. In contrast, other studies did not identify an association between prolonged CT and perioperative transfusion [3, 4]. We demonstrated that the proportion of transfused patients was significantly higher in the prolonged CT group than in the normal CT group, and that this difference was significantly amplified when we compared patients with prolonged CT according to both CEPI and CADP with the normal CT group.

Our study, which included all patients who had undergone surgery at a university hospital over a one-year period, demonstrates that a substantial portion of patients exhibited prolonged CT and that prolonged CT on PFA-200 was significantly associated with perioperative blood transfusion in surgical patients.

Authors' Disclosures of Potential Conflicts of Interest

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

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