Baseline platelet count may predict short-term functional outcome of cerebral infarction

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Abstract
Background and aims: Platelets play an important role in homeostasis however, they have also been associated with increased mortality after myocardial infarction. In the present study, we investigated whether platelet count is associated with differences in the short-term prognosis at the time of hospital discharge and early neurological deterioration in ischemic stroke patients.

Methods: Patients with ischemic stroke were enrolled from among 661 cerebrovascular disease patients admitted between January 2018 and December 2020. Patients who received hyperacute treatment, had a pre-onset modified Rankin scale (mRS) ≥ 3, transient ischemic attack, or active malignant disease were excluded. The platelet count was divided into quartiles (Q1-4) according to the number of patients, and the relationship between platelet count and prognosis was assessed using multivariable analysis.

Results: In total, 385 patients were included in the study. Regarding the functional outcome by platelet count, there was a significant increase in mRS ≥ 3 at discharge in the Q4 (range: 243–1327 × 10^9/L, \( p = 0.013 \), ORs: 1.674, 95%CI: 1.253–6.681) group compared to the Q3 (range: 205–242 × 10^9/L) group even after adjusting for factors with \( P < 0.2 \) in univariate analysis. Furthermore, the frequency of neurological deterioration (NIHSS ≥ 4) within 1 week was significantly lower in the Q3 group than in the Q1 (range: 19–173 × 10^9/L) and Q4 groups even after adjustment (Q1; \( p = 0.020 \) ORs: 6.634, 95%CI: 1.352–32.557, Q4; \( p = 0.007 \) ORs: 8.765, 95%CI: 1.827–42.035).

Conclusion: Platelet count at onset may affect the prognosis of cerebral infarction and early neurological deterioration. This study may help clarify the pathogenesis of cerebral infarction to improve prognosis.

Keywords: Platelet count, Cerebral infarction, Neurological deterioration, Early prognosis, Risk factors

Introduction
Platelet count measurements are frequently performed in clinical practice to assess bleeding risk and thrombosis. Inter-individual differences in platelet counts are highly variable [1]; however, platelet counts in healthy individuals are usually stable and exhibit little intra-individual variability over time [2]. A platelet count of approximately 50–100 × 10^9/L is generally sufficient to maintain vascular integrity and prevent spontaneous bleeding. However, a normal platelet count is 150–400 × 10^9/L, suggesting that platelets have another function (e.g. homeostasis maintenance) other than hemostasis [3, 4]. Consistent with this, a series of reports suggested that platelets play a role in physiological responses such as angiogenesis, fibrogenesis, and immune responses [5–7]. Therefore, platelets not only reflect underlying disease, but platelet function may also influence disease morbidity and mortality. An abnormal platelet count is a poor prognostic...
factor in some patient groups such as critically ill patients [8] and cancer patients [9, 10]. Furthermore, platelet counts outside the reference range are associated with mortality in the elderly and general population [11–13]. Recently, a U-shaped relationship between platelet count and mortality in the elderly population was reported [14]. Platelet counts have previously been linked to cause-specific mortality from cancer and cardiovascular disease [14]. In the field of cerebral infarction, platelet-related factors, such as CD40 ligand, monocyte-platelet aggregate formation and platelet-derived von Willebrand factor, are correlated with poor functional prognosis in stroke patient serum study and basic animal study [15, 16]. Du et al. [17] reported that elevated platelet counts increase the risk of ischemic stroke. In addition, Ye et al. showed that median platelet count group showed good stroke prognosis with long-term rehabilitation, but this was not a simple linear correlation [18]. However, reports on the relationship between platelet count and prognosis and neurological symptom exacerbation after stroke are limited, and the relevance is unclear. In this study, we analyzed whether platelet count is associated with differences in the short-term prognosis at the time of hospital discharge and early neurological deterioration in cerebral infarction.

**Patients and methods**

**Patients**

The study population comprised 661 Japanese patients who were admitted to our neurology department at Juntendo University Hospital within 2 days of acute stroke between January 2018 and December 2020. Exclusion criteria were: diagnosed with transient ischemic attack (TIA), underwent intravenous tissue plasminogen activator/endoextravascular treatment or malignancy treatment, or had a modified Rankin scale (mRS) ≥ 3. When the patients recovered to the functional stage from the assistance-free stage, they were discharged from the hospital to home. The endpoint of the trial was discharge from the hospital, and the study endpoints were the rate of mRS 3–6 at discharge and early neurological deterioration within 1 week from onset.

**Background data and risk factors**

We retrieved the following information from the medical records of each patient to evaluate the short-term prognosis at the time of hospital discharge and subsequent deterioration: 1) demographic data, 2) vital signs at presentation and laboratory findings on admission, 3) medications being taken upon admission, with particular attention paid to anti-platelets, anti-coagulants, anti-hypertensives, and statins, 4) vascular risk factors for stroke such as hypertension (HT; systolic blood pressure [BP] > 140 mmHg, diastolic BP > 90 mmHg, or drug treatment for HT), dyslipidemia (DL; low-density lipoprotein [LDL] cholesterol level of > 140 mg/dl, high-density lipoprotein [HDL]-cholesterol level of < 40 mg/dl, triglyceride [TG] level of > 149 mg/dl, or drug treatment for DL), diabetes mellitus (DM; glycated hemoglobin [HbA1c] level of > 6.8%, or drug treatment for DM), a cardioembolic source according to the Trial of Org 10,172 in Acute Stroke Treatment (TOAST) classification [19], TIA, and smoking history (as reported by the patient and their family), 5) stroke mechanism according to the TOAST criteria [19], and 6) the baseline National Institutes of Health Stroke Scale (NIHSS) score [20], as recorded by stroke-trained neurologists that were certified in the application of the NIHSS on admission, at 7 days after admission, and upon discharge. The deterioration of neurological findings was defined as worsening of the NIHSS score by ≥ 4 points within 1 week of admission to the hospital. Brain computed tomography (CT)/magnetic resonance imaging (MRI) and electrocardiography were performed in all patients. Brain MRI was conducted in all applicable patients. We diagnosed brain infarction by focal hyper-intensity that was judged not attributable to normal anisotropic diffusion or magnetic susceptibility artifact.

Briefly, according to Japanese stroke guidelines, thrombosis was treated with dual antiplatelet therapy (often use aspirin 200 mg/day and clopidogrel 75 mg), with edaravone and argatroban in acute phase. For cardioembolic embolism, we use edaravone in acute phase, and stated anticoagulant after day 2–5 from stroke onset. For embolic stroke of undetermined source, we treat with aspirin and edaravone.

**Ethical consideration and statistical analysis**

The protocol of this retrospective study was approved by the Human Ethics Review Committee of Juntendo University School of Medicine. The data were analyzed with SPSS 17.0 (SAS Institute Inc., Cary, NC) and are expressed as mean ± SD values. All statistical analyses were performed using χ² test for categorical variables and Kruskal Wallis test for non-parametric analyses. The platelet count was divided into quartiles and used in the multiple logistic regression analysis to estimate the relationship. Variables with a P value < 0.2 on univariate analysis were entered into multiple logistic regression analysis. p-values of < 0.05 were considered significant.

**Results**

A total of 385 patients were enrolled in this study after excluding patients who were diagnosed with hemorrhagic stroke (n = 91), TIA (n = 41), undergoing malignancy treatment (n = 56), mRS ≥ 3 (n = 46), or receiving
intravenous tissue plasminogen activator treatment and endovascular treatment ($n = 42$) (Fig. 1). Based on the final diagnosis using TOAST criteria, the following stroke subtypes were confirmed: small-vessel occlusion (SVO, $n = 50$, 13.0%), large-artery atherosclerosis (LAS, $n = 47$, 12.2%), cardioembolism (CE, $n = 107$, 27.8%), and other determined etiology (branch atheromatous disease [BAD], $n = 68$, 7.3%). Early neurological deterioration of NIHSS $\geq 4$ within 1 week from onset was noted in 35 patients (9.1%).

The patient background by platelet count quartiles is shown in Table 1 (range $\times 10^9$/L; Q1 19–173, Q2 174–204, Q3 205–242, Q4 243–1327, mean $\pm$ SD $\times 10^9$/L: overall mean 215 $\pm$ 86, Q1 = 138 $\pm$ 31, Q2 = 190 $\pm$ 9, Q3 = 223 $\pm$ 11, Q4 = 307 $\pm$ 117). Between quartiles, body mass index, smoking habit, and systolic blood pressure significantly differed ($p < 0.05$), but age, sex, HT, DM, DL, ischemic heart disease (IHD), atrial fibrillation (Af), history of cerebral infarction, and NIHSS on onset were not different. Stroke subtypes (SVO, LAS, CE, and BAD) and premedication from stroke onset did not differ, except for ARB medication ($p < 0.05$). Regarding laboratory findings (Table 2), white blood cell count, D-dimer, and N-terminal pro-brain natriuretic peptide (NT-proBNP) levels significantly differed ($p < 0.05$), but age, sex, or $\text{HbA1c}$ at admission. In patient outcome (Table 3), mRS $\geq 3$ (mRS3-6) at discharge and early neurological deterioration significantly differed between platelet quartiles ($p < 0.05$). However, antiplatelet therapy and anticoagulant therapy for secondary prevention were not differed in platelet query groups.

To investigate the relationship between platelet count and patient outcome, we analyzed the patient background factors that were relevant to mRS $\geq 3$ at discharge and early neurological deterioration. Univariate analysis revealed mRS $\geq 3$ (Table 4), sex, age, smoking habit, dyslipidemia, Af, NIHSS $\geq 8$, and WBC count were significant ($p < 0.2$). In stroke subtype, SVO and CE were significant ($p < 0.2$). We previously reported a good prognosis in patients taking angiotensin II receptor blocker (ARB) medication, and another report demonstrated that factors [21], such as statins and dipeptidyl peptidase 4 inhibitor/glucagon-like peptide-1 (DPP4/GLP-1) medication, were associated with prognosis [22]. Therefore, we analyzed premedication factors. Among premedication factors, ACE-I, statin, and diuretics were significant ($p < 0.2$). Likewise, early neurological deterioration was related ($p < 0.2$) to the factors of NIHSS $\geq 8$, WBC count, Hb count, SVO, LAS, BAD, and anticoagulant premedication in univariate analysis (Table 5).

We performed logistic regression analysis of factors related to mRS3-6 and deterioration between platelet count query groups (Table 6). Due to the U-shaped relationship between platelet count and prognosis [14], and mean platelet count being $215 \times 10^9$/L, we set the reference group as Q3. Factors that showed $p < 0.2$ in the univariate analysis were entered into the multivariable analysis. Regarding mRS3-6, with the reference set as Q3, the Q4 group had a significantly poorer prognosis ($p < 0.05$), and the Q1 group tended to have poor prognosis ($p = 0.079$). In the case of early neurological deterioration, the Q1 and Q4 groups had a higher rate than the Q3 group ($p < 0.05$).

**Discussion**

This study demonstrated the relationship between platelet count and ischemic stroke prognosis at discharge/early neurological deterioration. The Q3 group (range: 205–242 $\times 10^9$/L, mean $\pm$ SD: 223 $\pm 11 \times 10^9$/L) exhibited a low rate of early neurological deterioration and good prognosis compared with the Q1 and Q4 groups.

Our study is consistent with previous studies. One cohort study reported that platelet counts at the upper end of the normal range (301–450 $\times 10^9$/L) were associated with the development of cardiovascular disease [23], and the risk of ischemic stroke, myocardial infarction, and peripheral vascular disease were found to increase with platelet counts over $251 \times 10^9$/L. A cohort study of 1506 men reported an association between the risk of ischemic stroke and platelet counts in the upper normal range [24]. The relationship between platelet count and prognosis is gradually becoming one of the focal points of clinical research [13, 23]. An analysis based on 3229 subjects from the Chinese Acute Ischemic Stroke
Antihypertensive Study suggested that platelet count, especially the decrease due to platelet consumption, is an important non-negligible indicator in the prognosis of ischemic stroke [25]. It is well known that platelet activation is central to the process of arterial thrombus formation at the site of vascular injury [26]. Hence, antiplatelet therapy in arterial thromboembolism has received much attention, as antiplatelet agents prevent cerebrovascular disorders and cardiovascular events [26]. In addition, cardiovascular mortality increases in individuals with high platelet counts, especially in men and the elderly [14]. As reflected in these findings, our study also showed high platelet count group often occur neurological deterioration and appeared poor prognosis, even in no differences in stroke severity at onset between the groups based on the NIHSS score.

We found that early neurological deterioration in the low-platelet group (Q1) was significantly higher than the normal group, without stroke severity at onset. On the other hand, D’Erasmo et al. indicated the difference in platelet counts between the acute and recovery phases of stroke was not significant [27]. Several study suggests decreased platelet count is considered to be one of the risk factors for cerebral infarction [28]. Therefore, it is speculated that patients with low platelet counts often present with more obvious residual dysfunction, often

| Platelet quartiles | Q1 (96) | Q2 (96) | Q3 (96) | Q4 (97) |
|--------------------|---------|---------|---------|---------|
| Platelet count range (× 10^9/L) | 138±31 | 190±9 | 223±11 | 307±117 |
| 19–173 | 174–204 | 205–242 | 243–1327 |
| N | 60 | 65 | 64 | 56 |
| % | 62.5 | 67.7 | 66.7 | 57.7 |
| P-value | 0.480 | 0.071 | 0.004 | 0.006 |

| Values are expressed as mean ± SD except for NIHSS which is expressed as the median |
|---------------------|-------------------|
| BMI | body mass index, sBP | systolic blood pressure, dBP | diastolic blood pressure, IHD | ischemic heart disease, Af | atrial fibrillation, history of CI | history of cerebral infarction, NIHSS | National Institutes of Health Stroke Scale, SVO | small-vessel occlusion, LAS | large-artery atherosclerosis, CAD | carotid artery disease, CaB | calcium channel blocker, ARB | angiotensin II receptor blocker, ACE-I | angiotensin-converting-enzyme inhibitor, DPP4 | dipeptidyl peptidase 4 inhibitor, GLP1 | glucagon-like peptide-1 |

| sex (male) | 60 | 65 | 64 | 56 |
| age | 71.8±14.7 | 69.7±15.0 | 69.0±13.8 | 67.1±14.1 |
| BMI | 22.9±3.7 | 23.7±3.21 | 24.5±3.5 | 22.8±3.3 |
| smoking habit | 13 | 25 | 13 | 29 |
| hypertension | 67 | 69.8 | 81 | 72 |
| sBP | 147.5±28.5 | 152.5±25.1 | 160.5±29.0 | 155.1±32.2 |
| dBP | 83.6±17.7 | 85.6±14.5 | 90.0±19.7 | 89.2±19.4 |
| diabetes | 44 | 43 | 37 | 34 |
| dyslipidemia | 71 | 73 | 70 | 70 |
| IHD | 10 | 10 | 10 | 10 |
| Af | 28 | 24 | 20 | 22 |
| history of CI | 13 | 13.5 | 13.5 | 18 |
| NIHSS ≥ 8 | 15 | 10 | 13 | 9 |
| NIHSS | 4.8 | 3.2 | 3.9 | 3.5 |

| Stroke subtype | SVO | 6 | 16 | 29 | 6 |
| LAS | 16 | 6 | 10 | 25 | 7 |
| CE | 29 | 6 | 10 | 26 | 7 |
| BAD | 6 | 10 | 13 | 13 | 21 |

| Pre-medication | CaB | 21 | 16 | 15 | 28 |
| ARB | 16 | 23 | 32 | 33.3 |
| ACE-I | 8 | 2 | 3 | 3.1 |
| diuretics | 15 | 6 | 6 | 4.1 |
| statins | 28 | 33 | 30 | 31.3 |
| DPP4/GLP1 | 19 | 14 | 15 | 19.6 |
| anticoagulant | 17 | 20 | 9 | 13 |
| antiplatelet | 23 | 24 | 21 | 18.6 |

| Values expressed as mean ± SD except for NIHSS which is expressed as the median |
|---------------------|-------------------|
| BMI | body mass index, sBP | systolic blood pressure, dBP | diastolic blood pressure, IHD | ischemic heart disease, Af | atrial fibrillation, history of CI | history of cerebral infarction, NIHSS | National Institutes of Health Stroke Scale, SVO | small-vessel occlusion, LAS | large-artery atherosclerosis, CAD | carotid artery disease, CaB | calcium channel blocker, ARB | angiotensin II receptor blocker, ACE-I | angiotensin-converting-enzyme inhibitor, DPP4 | dipeptidyl peptidase 4 inhibitor, GLP1 | glucagon-like peptide-1 |
with early neurologic exacerbations. In a previous basic study using stroke-prone spontaneously hypertensive rats, a lower platelet count was a predictor of asymptomatic cerebral small vessel disease and symptomatic stroke [29]. Thus, both clinical reports and basic studies suggest that low and high platelet counts are associated with cerebral infarction.

Recently, Vinholt and colleagues concluded that platelet counts are associated with cardiovascular and cerebrovascular disease [23]. In general, cerebral infarction is closely related to platelet function, and thrombosis is the result of activation of platelets and the coagulation system. Thus, platelet count and function may have a significant impact on the occurrence and development of cerebral infarction [17]. Atherosclerosis is the pathologic basis of cerebral infarction, especially SVO, LAS, and BAD. As atherosclerosis progresses, endothelial cells in the vessel wall are damaged. As a result, the contact area with platelets increases, and thrombosis is more likely to be induced [29]. Platelets have also been shown to influence the effect of homocysteine on the prognosis of ischemic stroke. Increased homocysteine blood levels in patients with decreased platelet counts increase ischemic stroke mortality, but not in patients with normal to increased platelet counts [25]. Moreover, normal platelets play an important role in cell proliferation, chemotaxis, cell differentiation, and angiogenesis by releasing natural cytokines. The basic cytokines identified in platelets include transforming growth factor-β, platelet-derived growth factor, basic fibroblast growth factor, vascular endothelial growth factor, and endothelial cell growth factor [30]. Thus, it can be inferred that the factors that regulate the cellular environment produced by platelets affect the prognosis of cerebral infarction.

### Table 2  Laboratory data on admission

| Platelet quartiles | Platelet count (× 10^9/L) | Q1 (96) | Q2 (96) | Q3 (96) | Q4 (97) | P-value |
|-------------------|--------------------------|--------|--------|--------|--------|--------|
| range             | 19–173                   | 138±31 | 190±9  | 223±11 | 307±117|        |
| WBC               |                          | 6336±214| 6861±2648| 7368±2380| 7758±2840| 0.001  |
| Hb                |                          | 13.44±2.18| 14.09±1.96| 14.02±2.04| 14.39±2.13| 0.059  |
| hsCRP             |                          | 1.45±0.475| 0.501±1.425| 0.764±2.031| 1.260±3.744| 0.284  |
| PT-INR            |                          | 1.07±0.17| 1.25±1.32| 1.04±0.12| 1.08±0.34| 0.103  |
| D-dimer           |                          | 3.40±3.65| 2.21±2.46| 2.25±2.25| 2.32±2.39| 0.015  |
| eGFR              |                          | 64.1±27.1| 66.1±22.3| 63.0±24.0| 72.4±26.5| 0.100  |
| UA                |                          | 5.46±1.58| 5.56±1.44| 5.81±1.60| 1.58±1.58| 0.350  |
| HDL               |                          | 51.4±15.0| 53.1±13.5| 51.5±15.1| 54.5±17.5| 0.404  |
| LDL               |                          | 110.4±40.0| 112.3±39.3| 116.2±31.8| 122.9±48.6| 0.163  |
| TG                |                          | 136.9±86.5| 138.4±93.0| 145.8±106.6| 138.6±94.2| 0.981  |
| blood sugar       |                          | 144.5±72.8| 138.7±60.6| 131.5±43.9| 126.6±51.9| 0.287  |
| HbA1c             |                          | 6.67±1.86| 6.57±1.50| 6.40±1.29| 6.38±1.47| 0.365  |
| hsproBNP          |                          | 223.3±491.13| 902.5±2551.8| 1594.7±4967.2| 1122.17±5881.3| 0.004  |

### Table 3  Patient outcomes and anti-platelet/coagulant therapy for secondary prevention at discharge in platelet quartiles

| Platelet quartiles | Platelet count (× 10^9/L) | Q1 (96) | Q2 (96) | Q3 (96) | Q4 (97) | P-value |
|-------------------|--------------------------|--------|--------|--------|--------|--------|
| range             | 19–173                   | 138±31 | 190±9  | 223±11 | 307±117|        |
| mRS3-6            |                          | 22     | 10     | 10     | 25     | 0.004  |
| deterioration     |                          | 12     | 7      | 2      | 14     | 0.013  |
| Medication for secondary prevention | | | | | | |
| anticoagulant     |                          | 42     | 40     | 34     | 39     | 0.681  |
| antiplatelet      |                          | 55     | 56     | 53     | 51     | 0.859  |
Table 4  Univariate analysis of mRS at discharge

| Stroke subtype | mRS0-2 (318) | mRS3-6 (67) | P-value |
|----------------|-------------|-------------|---------|
| N             | %           | N           | %       |         |
| sex (male)    | 208         | 65.4        | 37      | 55.2    | 0.125   |
| Age           | 67.8 ± 14.2 | 77.18 ± 13.4| 0.441   |
| BMI           | 22.6 ± 3.50 | 22.58 ± 3.50| 0.380   |
| smoking habit | 68          | 21.8        | 12      | 17.9    | 0.620   |
| hypertension  | 236         | 74.2        | 53      | 79.1    | 0.441   |
| diabetes      | 134         | 42.1        | 24      | 35.8    | 0.412   |
| dyslipidemia  | 241         | 75.7        | 43      | 64.1    | 0.066   |
| IHD           | 30          | 9.4         | 8       | 11.9    | 0.504   |
| AF            | 68          | 21.3        | 26      | 38.8    | 0.004   |
| history of CI | 49          | 15.4        | 11      | 16.4    | 0.853   |
| NIHSS ≥ 8     | 18          | 5.6         | 29      | 43.2    | <0.001  |
| WBC           | 6940 ± 2510 | 7761 ± 2732 | 0.017   |
| Hb            | 13.7 ± 2.07 | 13.6 ± 2.22 | 0.649   |

Table 5 Univariate analysis on neurological deterioration within 7 days from onset

| Neurological deterioration | - (350) | + (35) | P-value |
|----------------------------|---------|--------|---------|
| N             | %       | N      | %       |         |
| sex (male)    | 224     | 64.0   | 21      | 60.0    | 0.713   |
| age           | 69.0 ± 14.3| 73.7 ± 15.4| 0.318   |
| BMI           | 23.5 ± 3.43| 23.6 ± 4.33| 0.220   |
| smoking habit | 72       | 20.5   | 8       | 22.8    | 0.827   |
| hypertension  | 264      | 75.4   | 25      | 71.4    | 0.682   |
| diabetes      | 147      | 42.0   | 11      | 31.4    | 0.280   |
| dyslipidemia  | 259      | 74.0   | 25      | 71.4    | 0.693   |
| IHD           | 37       | 10.45  | 1       | 2.8     | 0.231   |
| AF            | 84       | 24.0   | 10      | 28.5    | 0.540   |
| history of CI | 49       | 14.0   | 11      | 31.4    | 0.853   |
| NIHSS ≥ 8     | 37       | 10.5   | 10      | 28.5    | 0.005   |
| WBC           | 7048 ± 2555| 7452 ± 2674| 0.181   |
| Hb            | 13.8 ± 2.07| 13.2 ± 2.27| 0.161   |

Limitations
Our study has several limitations involving its non-random treatment allocation procedure and retrospective design. It must be emphasized that this study is exploratory; thus, we aimed to generate hypotheses, but not to test them. Second, antiplatelet and anticoagulant therapy were administered in combination with antihypertensive drugs, statins, and antidiabetic drugs in some patients. This treatment approach may have reduced the severity of stroke by reflecting more advanced medical measures and more aggressive risk factor reduction. Third, because the study was retrospective, information on duration of treatment and daily medication compliance was not available. Fourth, we were unable to determine how different treatment and imaging modalities for acute ischemic stroke influenced our results. However, as the patients in this study were treated for ischemic stroke according to Japanese stroke guidelines, the impact of such differences in treatment was estimated to be limited. Fifth, in generally, this type of analysis would be better to use fractional polynomials or restricted cubic splines. The main research question of this paper was the relationship between platelet count and prognosis, we selected categorical data for importance of U-shape curve. Further prospective randomized studies are needed to address these uncertainties.
Table 6  Logistic regression analysis for mRS3-6 and neurological deterioration

| PltQ | P-value | Odds   | 95%CI  | PltQ | P-value | Odds   | 95%CI  |
|------|---------|--------|--------|------|---------|--------|--------|
| Q1   | 0.079   | 2.159  | 0.914–5.101 | Q1   | 0.202   | 6.634  | 1.352–32.557 |
| Q2   | 0.837   | 1.107  | 0.422–2.900 | Q2   | 0.078   | 4.433  | 0.848–23.164 |
| Q3   | ref     |        |        | Q3   | ref     |        |        |
| Q4   | 0.013   | 1.674  | 1.253–6.681 | Q4   | 0.007   | 8.765  | 1.827–42.035 |

PltQ, platelet quartiles; mRS3-6, modified Rankin scale ≥ 3
including factors with p < 0.2 by univariate analysis
mRS3-6; sex, dyslipidemia, CE, ACE premedication, diuretics premedication, statin premedication, WBC, Af, NIHSS > 8
deterioration; anticoagulant therapy, SVD, ATBI, BAD, WBC, Hb, NIHSS > 8

Conclusion
In conclusion, lower and higher platelet counts at onset may affect the prognosis of cerebral infarction. Our clinical study demonstrated a U-curve. Maintaining a healthy platelet count may improve the prognosis of cerebrovascular disease. This may improve our understanding of the pathophysiology to help improve the prognosis of stroke.

Abbreviations
TIA: Transient ischemic attack; mRS: Modified Rankin scale; HT: Hypertension; BP: Blood pressure; DL: Dyslipidemia; LDL: Low-density lipoprotein; HDL: High-density lipoprotein; TG: Triglyceride; DM: Diabetes mellitus; HbA1c: Glycated hemoglobin; TOAST: Trial of Org 10,172 in Acute Stroke Treatment; NIHSS: National Institutes of Health Stroke Scale; CT: Computed tomography; MRI: Magnetic resonance imaging; SVO: Small vessel occlusion; LAS: Large-artery atherosclerosis; CE: Cardiogenic embolism; BAD: Branch atheromatous disease; MRA: Magnetic resonance angiography; SVD: Subcortical vascular disease; BAD: Branch atheromatous disease; WBC: White blood cell; Hb: Hemoglobin; NIHSS: National Institutes of Health Stroke Scale; SVD: Subcortical vascular disease; Hb: Hemoglobin; ADMI: Anterior cerebral artery disease; Af: Atrial fibrillation; NIHSS: National Institutes of Health Stroke Scale; PT-INR: Prothrombin time-international normalized ratio; UA: Uric acid; PltQ: Platelet quartiles.

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Authors’ contributions
Conceptualization, KK, NM; Methodology, NM, KH, YU; Investigation, KK, NM, KH, CK, YU; Formal analysis, NM, YU; Resources, NM, YU; Writing—original draft, KK, CK, YU; Writing—review and editing, all authors; Supervision, YU, NH. The author(s) read and approved the final manuscript.

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Availability of data and materials
The datasets used analyzed during the current study are available from the corresponding author on reasonable request.

Declarations
Ethics approval and consent to participate
The protocol of this retrospective study was approved by the Human Ethics Review Committee of Juntendo University School of Medicine. The patients provided their written informed consent to participate in this study.

All methods were carried out in accordance with relevant guidelines and regulations.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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