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Original Article

Different Long-Term Outcomes According to Thrombus Histology in Patients With Acute Ischemic Stroke

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Background and Purpose The relationship between thrombus histology and long-term stroke patient outcomes remains unexplored. We aimed to determine whether the histological characteristics of thrombi are associated with long-term outcomes in stroke patients and to identify the thrombus features linked to these outcomes.

Methods This retrospective multicenter cohort study included 512 patients with ischemic stroke who underwent endovascular thrombectomy between July 2017 and July 2023. Patients were followed up for long-term major adverse cardiovascular events occurrence. Thrombus histology was assessed using immunohistochemistry, including the proportion of fibrin, red blood cells, and platelets, as well as the distribution patterns categorized as layered, erythrocytic, diffuse platelet, and mixed.

Results During a median follow-up of 38.1 months, 164 patients experienced major adverse cardiovascular events, with an incidence rate of 3.02 per 100 person-years. Major adverse cardiovascular events occurrence was associated with the diffuse platelet pattern and proportion of platelets and red blood cells within the thrombus. After adjusting for confounders, the diffuse platelet pattern independently predicted major adverse cardiovascular events, including mortality and stroke recurrence. Subgroup analysis also demonstrated that the association between the diffuse platelet pattern and major adverse cardiovascular events was consistent across key clinical subgroups based on age (≥65 vs. <65 yr), atrial fibrillation, cancer status, and discharge medications.

Conclusions Thrombus histology could provide predictive value for long-term prognosis. In particular, histological distribution patterns may be more important than simple composition in thrombus research, including in the prediction of prognosis.

Keywords Ischemic stroke; Major adverse cardiovascular events

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Introduction

Ischemic stroke is a representative thrombotic disease. Since the advent of endovascular thrombectomy (EVT), numerous studies have been conducted due to its ability to retrieve thrombi. Previous studies have primarily focused on understanding the mechanisms underlying ischemic stroke, the efficacy of thrombolytic therapy, and outcomes of EVT based on thrombus histology.[1-3]

However, the mechanism of thrombus formation varies among patients.[4,5] Thrombus characteristics, such as composition and structural patterns, are likely associated with the underlying vascular, hemodynamic, and systemic conditions. These factors are reflected in the thrombus itself. As the response to treatments aimed at dissolving or retrieving the thrombus depends on its histological characteristics, the response to antithrombotic agents may also vary. Therefore, understanding these diverse characteristics could provide insights into differences in long-term outcomes. Although prior works have focused on compositional fractions and short-term outcomes (e.g., discharge or 90-day functional outcome),[6,7] the relationship between morphology-based thrombus patterns and long-term cardiovascular events has not been established.

This study aimed to determine whether the histological characteristics of thrombus are associated with long-term outcomes in patients, identify which specific thrombus properties are linked to these outcomes, and investigate the utility of thrombus-based analysis in predicting the prognosis of patients with stroke.

Methods

Data availability

Anonymized data not published within this article will be made available by request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Study population

This retrospective study utilized data from the Specialized Multi-Center Attributed Registry of Stroke–CLOT (SMART-CLOT), a prospective nationwide multicenter registry that includes patients with acute consecutive ischemic stroke from 13 centers in South Korea who underwent EVT due to large vessel occlusion.[8] Each participating center maintains a site-specific de-identified unique patient identifier, which enabled within-center linkage of encounters from the same individual. When more than one EVT with thrombus retrieval occurred for a patient at the same center during the study period, only the first (index) EVT thrombus and its corresponding clinical data were retained; subsequent EVTs were not analyzed as separate index entries. To assess the possibility of cross-center re-registration, we reviewed baseline histories of previous stroke and queried the registry for evidence of prior EVT with thrombus retrieval. Among 34 patients with a previous stroke history, none had a prior EVT, confirming that all analyzed thrombi correspond to index EVTs of unique patients. Reperfusion therapy was performed using protocols based on the guidelines. In addition, during hospitalization at the study hospitals, all patients underwent a comprehensive assessment that included medical history, blood tests, computed tomography, magnetic resonance imaging, carotid ultrasonography, transcranial Doppler, 12-lead electrocardiography (EKG), echocardiography, Holter monitoring, and continuous EKG monitoring.

Standard protocol approvals, registrations, and patient consents

Written informed consent was obtained from prospectively enrolled patients or their legal representatives. The Institutional Review Board approved the registry of each participating hospital. For this study, we included patients from 5 of the 13 participating centers (Seoul Medical Center, Yongin Severance Hospital, Ewha Woman's University Seoul Hospital, National Health Insurance Service Ilsan Hospital, and Severance Hospital), as these centers currently have data on long-term outcomes. This study was approved by the Institutional Review Board of Yonsei University College of Medicine (approval number: 4-2024-1662).

Thrombus preparation and immunohistochemistry

Thrombi retrieved from EVT were promptly placed in tubes containing 4% paraformaldehyde and fixed overnight at 4°C. Subsequently, all thrombi were transported immediately to the central laboratory at Yonsei University College of Medicine. They were processed into paraffin blocks and stored until analysis. Using these paraffinized blocks, the thrombi composition was subsequently analyzed using immunohistochemistry.

The paraffin-embedded thrombi were sectioned into 3-μm-thick slices. Following deparaffinization and blocking with 1% horse serum and 5% non-fat milk in Tris-buffered saline, the sections were incubated overnight at 4°C with primary antibodies. For immunohistochemistry, the following primary antibodies were used: monoclonal anti-CD42b (ab134087, 1:100; Abcam, Cambridge, UK) for platelets, rabbit polyclonal anti-fibrinogen (ab34269, 1:200; Abcam) for fibrin/fibrinogen, and rabbit monoclonal anti–glycophorin A (ab129024, 1:400; Abcam) for red blood cells (RBCs). Antigen retrieval was performed using the IHC-Tek epitope retrieval solution and a steamer (IHC World, Woodstock, MD, USA), except for anti-CD42b. Secondary antibody binding was performed using the avidin-biotin-horseradish peroxidase complex (Vector Laboratories, Peterborough, UK),

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followed by color development with 3,3′-diaminobenzidine. Hematoxylin counterstaining was conducted, and the slides were mounted with Permount Mounting Medium (Fisher Scientific, Fair Lawn, NJ, USA).

Assessment of thrombus characteristics

In this study, thrombi from individual patients were analyzed based on various characteristics, including the proportion of primary thrombus components such as RBCs, fibrin, and platelets. Whole-slide images of stained thrombi were acquired using a whole-slide scanner (MoticEasyScan Pro 6; Motic Hong Kong Limited, Hong Kong, China) at 40× (0.26 μm/pixel). The scanned images were analyzed using the Automated Region-of-Interest-Based Image Analysis, open-source software for automated composition analysis.[9] A fixed threshold was applied, and the proportions of RBCs, platelets, and fibrin/fibrinogen were calculated as the percentage of pixel density relative to the total thrombus area.

The thrombus distribution patterns were subsequently analyzed. The extracted thrombi were categorized into four groups based on their overall distribution patterns of common components of thrombus, especially platelets and RBCs, as described in previous reports (Figure 1).[10,11] The platelet distribution pattern was the most distinctive. First, a layered pattern was defined when platelets were linearly deposited in layers or clustered in spots within the thrombus.[10,11] Second, some thrombi exhibited an erythrocytic pattern, where platelets were predominantly located at the periphery, with densely packed RBCs in the core.[10,11] Third, a diffuse platelet pattern was defined as a uniform distribution of platelets throughout the thrombus without any specific organization. A single dominant pattern was assigned when that pattern occupied ≥70% of the thrombus in the reviewed section. Specimens that did not meet this rule were classified as mixed pattern. Two investigators (H.L. and Y.D.K.) independently assessed the thrombus pattern without any clinical information and achieved good agreement ($\kappa_{un\text{-}weighted}$, 0.88; 95% confidence

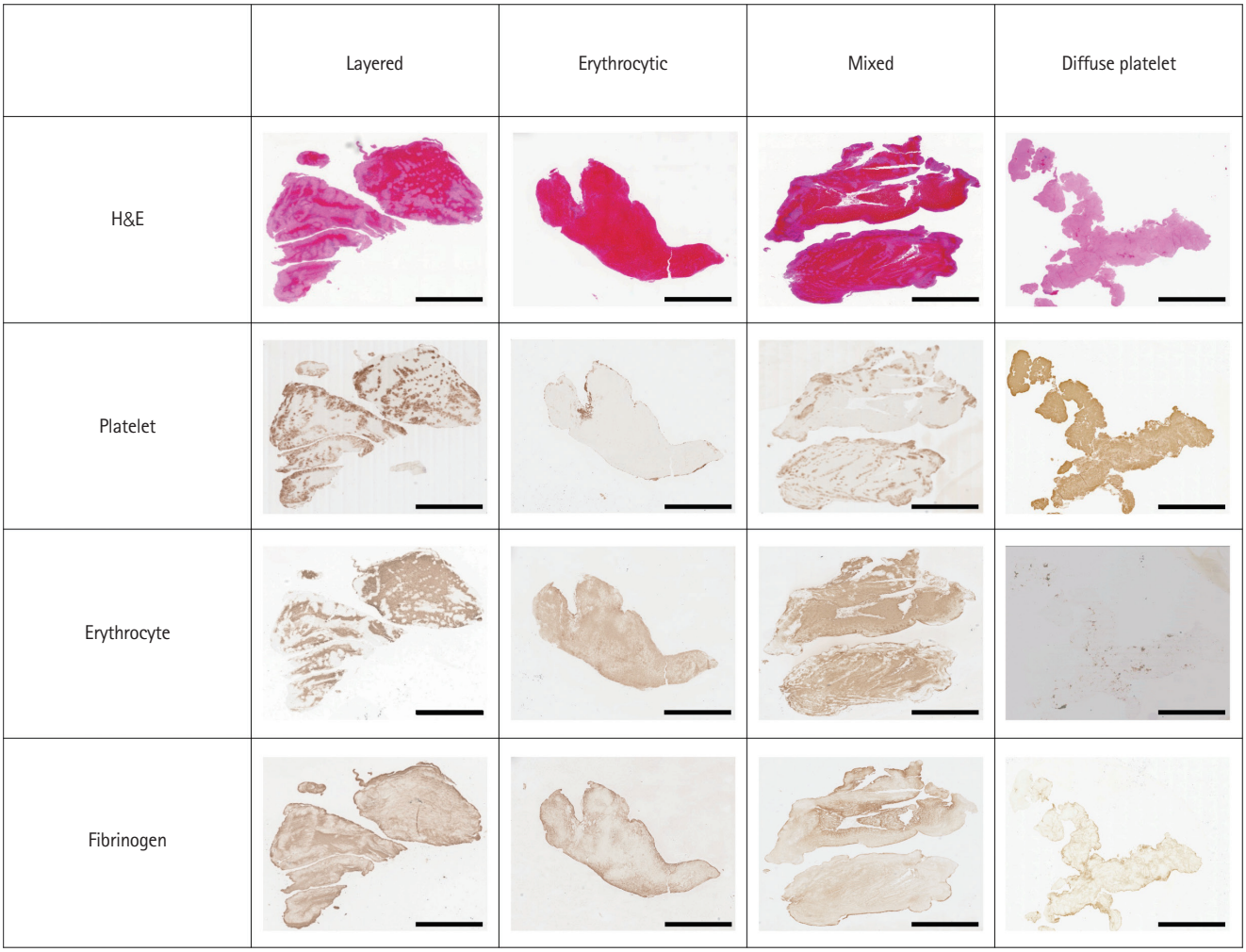

Figure 1. Representative immunohistochemical staining patterns of thrombi retrieved from ischemic stroke patients via mechanical thrombectomy. Scale bar=1 mm. H&E, hematoxylin and eosin.

interval [CI], 0.84–0.91). Any disagreements were resolved by consensus.

Clinical variables

We analyzed data on demographics, vascular risk factors, comorbidities, and laboratory results. Active cancer was defined as cancer diagnosis, recurrence, ongoing treatment within the past 6 months, inoperable cancer, or metastasis. Premorbid disability was defined as a modified Rankin Scale score of 2–5.[12] Stroke subtypes were classified according to the criteria of the Trial of Org 10172 in Acute Stroke Treatment.[13] Stroke severity was assessed using the National Institutes of Health Stroke Scale (NIHSS). Immediate modified Thrombolysis in Cerebral Infarction (mTICI) was defined as the angiographic reperfusion grade recorded on the final digital subtraction angiography run at the end of the EVT. Successful recanalization was defined as achieving the mTICI score of 2b or 3.

Outcome measure

The primary outcome measured in this study was major adverse cardiovascular events (MACE), defined as a composite of all-cause mortality, ischemic heart disease (IHD), and stroke (ischemic or hemorrhagic). Each event within the composite outcome was separately analyzed to compare individual incidences. The IHD events included acute myocardial infarction, unstable angina, percutaneous transluminal coronary angioplasty/stent placement, and coronary artery bypass grafting. Data on vascular events and death were collected through face-to-face or telephone interviews conducted by stroke specialists or stroke research nurses at 3, 6, 9, and 12 months after the index event. Medical chart reviews were conducted when necessary to supplement the interviews and, beyond 12 months, served as the primary source of longitudinal follow-up to capture MACE and its components. The censoring date was October 31, 2024. Patients with at least one post-discharge follow-up were included and, if event-free, censored at their last contact; individuals with no post-discharge information contributed no at-risk time and were excluded. Because deaths within 4 weeks of the index EVT are predominantly attributable to the acute index stroke and periprocedural course rather than longer-term thrombus biology, patients who died before day 28 were excluded by design.[14,15]

Statistical analysis

Data were presented as means±standard deviations, medians (interquartile ranges), or numbers (%), as appropriate. Continuous variables were compared between groups using the t-test, Kruskal–Wallis test, and Mann–Whitney U test. Associations between categorical variables were analyzed using the chi-squared or Fisher's exact test, as appropriate. MACE incidence rates were calculated as events per 100 person-years. Kaplan–Meier survival curves were used to estimate cumulative incidence, and the log-rank test was used to evaluate differences in thrombus patterns. Cox proportional hazards regression models assessed the association between thrombus characteristics and the risk of clinical events, including MACE. Hazard ratios (HRs) with 95% CI were reported.

Variables for the multivariable analyses were selected from significant univariable analyses (P<0.05). We assessed linearity of the log-hazard for each continuous covariate using Martingale residuals and restricted cubic splines (four knots). Based on Wald tests, age was modeled with restricted cubic splines (nonlinearity P=0.010); C-reactive protein (CRP)/D-dimer/glucose were natural log-transformed and entered linearly, and NIHSS and onset-to-recanalization were retained as linear terms. For continuous variables entered linearly, HRs represent the relative hazard associated with a one-unit increase in the covariate. For biomarkers that were natural log-transformed, HRs correspond to a one-unit increase in the natural log-transformed value. Because age was modeled using restricted cubic splines, HRs for age are presented as contrasts from the spline model, as noted in the table footnotes. For low-event endpoints (stroke and IHD), we conducted sensitivity analyses using Firth penalized Cox regression. To preserve degrees of freedom, adjustment was parsimonious: the stroke model included thrombus pattern, age (per 10 yr, linear), sex, active cancer, and initial NIHSS; the IHD model included thrombus pattern, age (per 10 yr, linear), and sex. The predictive performance of the multivariable model was assessed at 1, 3, and 5 years using the receiver operating characteristic (ROC) curve, and the area under the curve (AUC) was calculated to quantify the model's discriminative ability. Subgroup analyses were conducted to examine MACE risk based on age (≥65 vs. <65 yr), atrial fibrillation, cancer status, and discharge medications. Interaction terms were included to evaluate effect modification. A two-sided P<0.05 was considered statistically significant for all tests. All statistical analyses were conducted using the R software (version 4.4.2; R Foundation for Statistical Computing, Vienna, Austria).

Results

Among the initial 549 patients who underwent EVT with thrombi retrieved between July 2017 and July 2023 across 5 stroke centers, those who were lost to follow-up (n=19) and those who died within 4 weeks after stroke (n=18) were excluded. Accordingly, data from a total of 512 patients were included in the final analysis (Supplementary Figure 1).

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The mean age of the study population was 73.8±12.8 years, and 271 patients (52.9%) were male. Cardioembolism was the most common stroke mechanism, observed in 57.8% of the patients. Intravenous tissue plasminogen activator was administered to 192 patients (37.5%). The median onset-to-recanalization time was 5.5 hours, and successful thrombectomy was achieved in 470 patients (91.8%). Within thrombi, median proportions of RBCs, fibrin, and platelets were 36.1%, 32.6%, and 9.8%, respectively.

The layered pattern (n=203, 39.6%) was most common, followed by the mixed (n=134, 26.2%), erythrocytic (n=129, 25.2%), and diffuse platelet patterns (n=46, 9.0%). Patients with diffuse platelet pattern were more likely to be younger and to have cancer, higher CRP and D-dimer levels, and shorter onset-to-recanalization time (all $P<0.05$), compared with those with other patterns. Compared with patients with other patterns, patients with diffuse pattern showed a significantly higher proportion of platelets and a lower proportion of RBCs within the thrombus (all $P<0.05$), whereas fibrin composition did not differ significantly between patients with different patterns ($P>0.05$). The layered pattern was associated with atrial fibrillation ($P<0.05$). However, no difference based on thrombus pattern was observed in stroke severity or recanalization success ($P>0.05$) (Table 1).

During a median follow-up of 38.14 months (interquartile range, 12.69–54.75), a total of 164 patients experienced MACE, with 111 deaths, 63 strokes (60 ischemic and 3 hemorrhagic), and 11 cases of IHD reported. The annual MACE incidence rate was 3.02 per 100 person-years. Univariable Cox regression analysis revealed that the proportion of platelets (HR, 1.02; 95% CI, 1.01–1.03; $P=0.003$) and RBCs (HR, 0.99; 95% CI, 0.98–1.00; $P=0.020$) were associated with increased risk of MACE, whereas fibrin proportion was not ($P=0.300$). The diffuse platelet pattern was associated with a higher risk of MACE, compared with the layered pattern (Supplementary Table 1). Kaplan–Meier curves demonstrated significant differences in the cumulative incidence of MACE across the four thrombus patterns (log-rank test, $P<0.001$) (Figure 2).

The univariable analysis identified the following significant predictors of MACE: age, male sex, cancer, end-stage renal disease, hemoglobin level, CRP level, D-dimer level, initial glucose level, premorbid disability, initial NIHSS score, onset-to-recanalization time, successful recanalization, prescribed medication at discharge, as well as platelet and RBC proportions within the thrombus (all $P<0.05$) (Supplementary Table 1). Multivariable analysis revealed that diffuse platelet pattern remained an independent predictor of MACE (HR, 2.35; 95% CI, 1.11–4.98; $P=0.026$) after adjusting for multiple confounders. However, platelet and RBC compositions were not significant predictors of MACE after adjusting for confounders in the multivariable analysis ($P=0.529$ and $P=0.795$, respectively) (Supplementary Table 2).

As the risk of MACE varied according to distribution patterns, we conducted further analyses. Among the four patterns, the diffuse platelet pattern exhibited the highest incidence rate of MACE at 9.43 per 100 person-years, followed by the mixed pattern at 3.37, erythrocytic pattern at 2.82, and layered pattern at 2.14 (Figure 3). The diffuse platelet pattern was significantly associated with all-cause mortality (HR, 3.47; 95% CI, 1.49–8.07; $P=0.004$) and stroke occurrence (HR, 5.66; 95% CI, 1.59–20.20; $P=0.007$) (Table 2). The diffuse platelet pattern was also associated with higher all-cause mortality (6.96 per 100 person-yr) and stroke occurrence (4.19 per 100 person-yr), compared with the other patterns. Kaplan–Meier curves demonstrated that the diffuse platelet pattern was associated with the highest cumulative incidence of all-cause mortality and stroke occurrence during follow-up. IHD events were rare across all groups, with no occurrences reported in the diffuse pattern group. As a result, the incidence of IHD was insufficient to allow for a robust comparison between groups (Supplementary Figure 2). In sensitivity analyses using Firth-penalized Cox models with minimal adjustment, the diffuse platelet pattern showed a robust association with stroke (HR, 6.31; 95% CI, 2.74–14.08; $P<0.001$). In contrast, for IHD the estimates were imprecise and not statistically significant (HR, 0.48; 95% CI, 0.01–4.62; $P=0.586$), consistent with the small number of events (Supplementary Table 3). In an additional sensitivity analysis that included 18 patients who died within 4 weeks after the index event, the results were consistent with the primary analysis. The diffuse platelet pattern remained significantly associated with MACE, all-cause mortality, and stroke recurrence, confirming the robustness of our findings (Supplementary Table 4).

Subgroup analysis demonstrated that the association between the diffuse platelet pattern and MACE was consistent across key clinical subgroups, including those based on age (≥65 vs. <65 yr), atrial fibrillation, cancer status, and discharge medications (antiplatelet, anticoagulant, combination, or none) (Supplementary Figure 3). To further assess the predictive performance of the multivariable model in estimating MACE risk across different thrombus distribution patterns, we performed a time-dependent ROC curve analysis. The AUC values for MACE prediction at 1, 3, and 5 years were 0.796, 0.822, and 0.842, respectively, indicating a significant and progressive improvement in discriminative ability over time (Supplementary Figure 4).

Discussion

In this study, we evaluated the long-term outcomes of patients

Table 1. Comparison of baseline characteristics according to immunohistochemical staining patterns

	Entire population (n=512)	Layered (n=203)	Erythrocytic (n=129)	Mixed (n=134)	Diffuse platelet (n=46)	*P*
Age (yr)	73.8±12.8	74.1±12.5	74.7±11.6	74.7±13.3	66.8±14.0	0.001
Male sex	271 (52.9)	104 (51.2)	76 (58.9)	64 (47.8)	27 (58.7)	0.247
Hypertension	365 (71.3)	139 (68.5)	93 (72.1)	101 (75.4)	32 (69.6)	0.575
Diabetes mellitus	156 (30.5)	53 (26.1)	36 (27.9)	55 (41.0)	12 (26.1)	0.021
Dyslipidemia	171 (33.4)	82 (40.4)	36 (27.9)	38 (28.4)	15 (32.6)	0.051
CAOD	80 (15.6)	36 (17.7)	20 (15.5)	23 (17.2)	1 (2.2)	0.065
PAOD	15 (2.9)	9 (4.4)	2 (1.6)	4 (3.0)	0 (0.0)	0.276
Atrial fibrillation	272 (53.1)	122 (60.1)	64 (49.6)	72 (53.7)	14 (30.4)	0.003
Active cancer	37 (7.2)	8 (3.9)	4 (3.1)	4 (3.0)	21 (45.7)	<0.001
ESRD	7 (1.4)	3 (1.5)	2 (1.6)	2 (1.5)	0 (0.0)	0.872
Hemoglobin (g/L)	132.0 [118.0; 145.0]	132.0 [119.0; 146.0]	131.0 [120.0; 143.0]	134.0 [118.0; 147.0]	126.0 [107.0; 145.0]	0.390
White blood cell (10^9/L)	7.9 [6.5; 9.7]	7.9 [6.4; 9.7]	7.6 [6.5; 9.5]	8.2 [6.6; 9.5]	9.2 [6.7; 11.4]	0.126
Platelet (10^9/L)	201.5 [164.0; 244.0]	197.0 [164.0; 240.0]	199.0 [163.5; 241.0]	211.5 [174.0; 251.0]	188.0 [128.0; 252.0]	0.215
C-reactive protein (mg/L)	3.8 [1.5; 10.7]	3.3 [1.5; 9.0]	3.6 [1.2; 10.8]	3.9 [1.6; 10.7]	8.6 [3.6; 43.4]	0.003
D-dimer (nmol/L)	2.9 [1.2; 7.8]	2.7 [1.1; 6.5]	2.1 [1.1; 5.7]	3.0 [1.4; 8.6]	7.0 [2.0; 14.4]	0.018
Albumin (g/L)	40.0 [37.0; 43.0]	40.0 [36.0; 42.0]	39.0 [36.0; 42.0]	40.0 [38.0; 43.0]	40.0 [37.0; 43.0]	0.206
Initial glucose (mmol/L)	7.2 [6.2; 8.7]	7.2 [6.0; 8.7]	7.2 [6.2; 8.4]	7.3 [6.2; 8.7]	7.5 [6.2; 9.0]	0.564
Premorbid disability	216 (42.2)	69 (34.0)	56 (43.4)	65 (48.5)	26 (56.5)	0.008
Initial NIHSS	12.0 [7.0; 17.0]	13.0 [8.0; 17.0]	12.0 [7.0; 17.0]	13.0 [8.0; 18.0]	11.0 [7.0; 15.0]	0.162
IV tPA	192 (37.5)	91 (44.8)	36 (27.9)	49 (36.6)	16 (34.8)	0.019
Stroke classification						<0.001
Cardioembolic	296 (57.8)	145 (71.4)	61 (47.3)	74 (55.2)	16 (34.8)	
LAA	83 (16.2)	18 (8.9)	30 (23.3)	25 (18.7)	10 (21.7)	
Other	133 (26.0)	40 (19.7)	38 (29.5)	35 (26.1)	20 (43.5)	
Onset to recanalization (hr)	5.5 [3.6; 9.8]	4.6 [3.2; 8.2]	6.8 [4.4; 10.9]	5.3 [3.6; 10.6]	4.5 [3.4; 9.4]	0.002
Modified TICI ≥2b	470 (91.8)	192 (96.0)	114 (90.5)	124 (93.2)	40 (87.0)	0.084
Discharge medication						<0.001
Anticoagulant	270 (52.7)	124 (61.1)	60 (46.5)	72 (53.7)	14 (30.4)	
Antiplatelet	160 (31.2)	45 (22.2)	49 (38.0)	47 (35.1)	19 (41.3)	
None	38 (7.4)	16 (7.9)	7 (5.4)	7 (5.2)	8 (17.4)	
Both	44 (8.6)	18 (8.9)	13 (10.1)	8 (6.0)	5 (10.9)	
Platelet (%)	9.8 [4.8; 18.8]	11.2 [7.5; 19.6]	4.4 [2.1; 9.7]	10.8 [5.5; 16.5]	40.1 [19.3; 61.3]	<0.001
Red blood cell (%)	36.1 [23.0; 46.5]	36.3 [23.3; 44.5]	39.3 [23.8; 49.8]	37.7 [28.9; 47.6]	6.1 [1.5; 29.1]	<0.001
Fibrin (%)	32.6 [20.7; 45.8]	34.6 [22.6; 45.2]	29.6 [17.3; 43.3]	32.5 [24.4; 47.8]	27.1 [8.4; 47.4]	0.090

Data are presented as n (%), mean±SD, or median [interquartile range].
CAOD, coronary artery occlusive disease; PAOD, peripheral artery occlusive disease; ESRD, end stage renal disease; NIHSS, National Institutes of Health Stroke Scale; tPA, tissue plasminogen activator; LAA, large artery atherosclerosis; TICI, Thrombolysis in Cerebral Infarction.

with acute ischemic stroke based on thrombus histological characteristics. Thrombus constituents, such as RBCs and platelets, were significantly related to MACE in the univariable analysis; however, their significance was lost after adjusting for potential confounders. In contrast, thrombus patterns, particularly the diffuse platelet pattern characterized by diffusely distributed platelets, were associated with a significantly higher incidence of MACE, all-cause mortality, and recurrent stroke over the long term. This association remained significant in multivariable analyses adjusted for confounders, such as comorbidities including cancer, and in subgroup analyses.

Most previous studies on human stroke thrombi have reported associations between clot histology and a wide range of clinical and radiographic parameters, including stroke mechanism, clinical presentation, imaging features, responsiveness to thrombolysis or EVT, clot migration, secondary embolism, and short-

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term functional outcomes.[1-3,16,17] However, none have examined whether histological characteristics are associated with long-term outcomes or prognosis. Considering that thrombus formation and underlying diseases are reflected in thrombus characteristics, which in turn may influence clinical presentation and outcomes, it is plausible that these characteristics could also be associated with long-term prognosis. In this study, we demonstrated that thrombus distribution patterns were strongly and independently associated with the risk of MACE, all-cause mortality, and recurrent stroke.

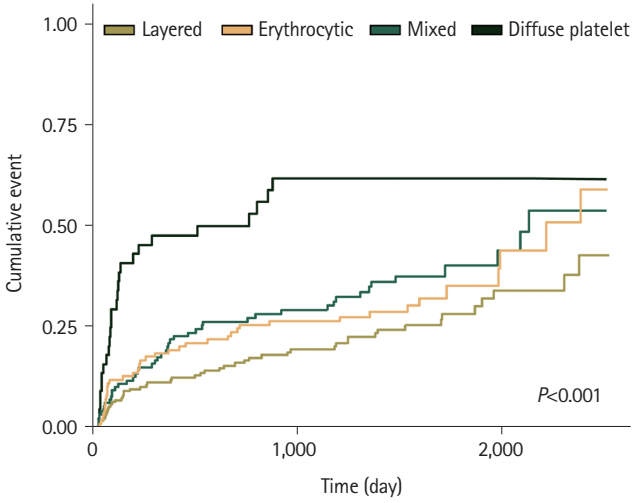

Figure 2. Cumulative Incidence of MACE by immunohistochemical staining patterns.

Previous studies primarily focused on measuring the fractional contents of RBCs, fibrin, and platelets, as comparing thrombus compositions has been the standard approach in thrombus research. In this study, we measured the compositional fractions of thrombi as a basic approach to identifying their characteristics. However, the specific compositions of RBCs, platelets, and fibrin were not independently correlated with long-term outcomes. Recent meta-analyses showed that although thrombus composition varies slightly depending on stroke mechanism, relying solely on thrombus composition for clinical applications has limitations.[16] Even with identical composition, distribution patterns of thrombus components can vary significantly because thrombosis can be influenced by factors, such as blood flow and local conditions at the site of thrombus formation.[4,10,18] Although many studies have attempted to determine thrombus patterns in relation to ischemic stroke mechanisms using hematoxylin and eosin staining,[10,18] accurate pattern assessments proved somewhat challenging. Additionally, the pattern classifications were not consistently applied.[16] We classified thrombus into four patterns, demonstrating that these patterns offer more valuable information than simple compositional analyses. Among these, the layered pattern demonstrated the best prognosis, whereas the diffuse platelet pattern was associated with the worst outcomes.

In areas of high shear stress, such as atherosclerotic stenosis, RBCs tend to aggregate, and platelets become activated in slow-

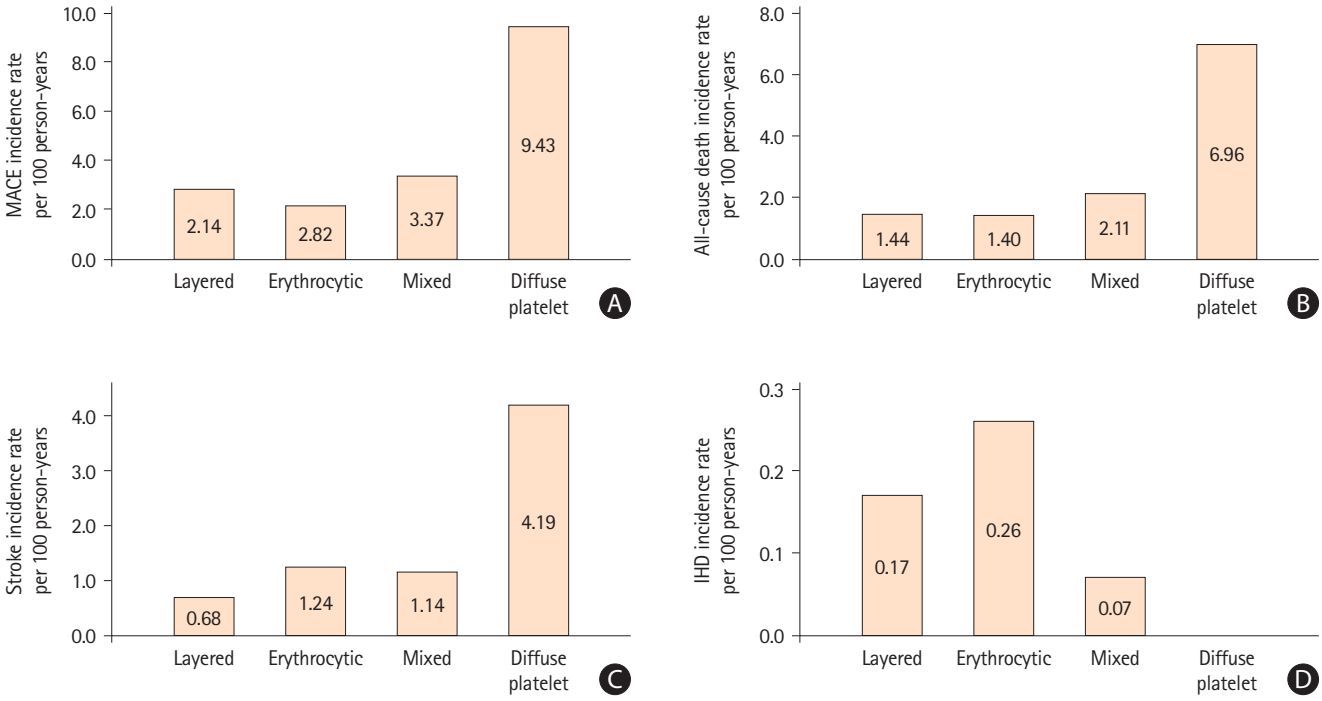

Figure 3. Incident rate of cardiovascular outcome stratified by immunohistochemical staining patterns. (A) Major adverse cardiovascular events (MACE). (B) All-cause death. (C) Stroke. (D) Ischemic heart disease (IHD).

Table 2. Multivariable-adjusted* analysis of cardiovascular outcomes based on immunohistochemical staining patterns

Outcome	Pattern	HR (95% CI)	*P*
MACE			
	Layered	Reference	
	Erythrocytic	1.23 (0.73–2.08)	0.436
	Mixed	1.44 (0.87–2.37)	0.152
	Diffuse platelet	2.35 (1.11–4.98)	0.026
All-cause death			
	Layered	Reference	
	Erythrocytic	0.89 (0.45–1.76)	0.738
	Mixed	1.39 (0.76–2.55)	0.290
	Diffuse platelet	3.47 (1.49–8.07)	0.004
Stroke			
	Layered	Reference	
	Erythrocytic	1.86 (0.75–4.60)	0.198
	Mixed	1.56 (0.63–3.90)	0.341
	Diffuse platelet	5.66 (1.59–20.20)	0.007
IHD			
	Layered	Reference	
	Erythrocytic	2.45 (0.22–17.38)	0.469
	Mixed	0.79 (0.05–12.88)	0.874
	Diffuse platelet	N/A	N/A

HR, hazard ratio; CI, confidence interval; MACE, major adverse cardiovascular events; IHD, ischemic heart disease; N/A, not applicable.
*Adjusted for age (restricted cubic splines, four knots), sex, active cancer, end stage renal disease, poor premorbid status, natural log-transformed biomarkers (C-reactive protein, D-dimer, initial glucose), initial National Institutes of Health Stroke Scale, onset to recanalization time, immediate modified Thrombolysis in Cerebral Infarction, discharge medication, platelet staining, and red blood cell staining.

er-moving post-stenotic segments, forming an erythrocytic pattern.[10] In cardioembolic conditions, such as atrial fibrillation, the layered pattern or clustered spots of platelet aggregates are often observed owing to the rapid and constant blood flow within the heart.[18] The better prognosis associated with the layered pattern may be explained by the availability of effective secondary prevention measures, such as non-vitamin K antagonist oral anticoagulants, for cardioembolic stroke.[19]

In our study, patients with the diffuse platelet pattern were younger and had shorter onset-to-recanalization times but had the poorest outcomes. Many of these patients had a history of cancer and elevated D-dimer levels, suggesting a potential link between poor prognosis and cancer. However, the association between the diffuse platelet pattern and poor prognosis remained significant even after subgroup analysis based on cancer status and stroke mechanism. No significant differences were observed between the patterns in terms of NIHSS scores on admission or recanalization success rates, which are major determinants of long-term prognosis after EVT.[20] These findings suggest that the characteristics of the diffuse platelet pattern are independently associated with poor prognosis, irrespective of comorbidities or EVT success.

Furthermore, approximately one-third of the patients with the diffuse platelet pattern had cardioembolic stroke and one-fifth had large artery atherosclerosis. These findings suggest that some patients may develop thrombi characterized by enhanced platelet activation irrespective of the underlying stroke mechanism. The role of platelets in thrombus formation in ischemic stroke is well established; they interact with RBCs, fibrin, and the von Willebrand factor, contributing to thrombus maturation, contraction, and formation of the outer shell.[21-25] Such thrombi have been reported to exhibit resistance to thrombolytic and reperfusion therapy. Considering that the hospitals participating in this study provided treatment in accordance with established guidelines, our results suggest that patients with diffuse platelet patterns may exhibit poor response to conventional antithrombotic therapies. This highlights the need for more effective treatment strategies for patients with this type of thrombus.

This study has some limitations. First, we did not include data on medication adherence or control of cardiovascular risk factors after discharge. Second, we only included patients who survived beyond 4 weeks after the index EVT, excluding those who died of acute index stroke or stroke complications. However, all participating hospitals were university or general hospitals that follow the recommended guidelines for secondary prevention and provide regular follow-up. This reduced the likelihood that our findings resulted from insufficient treatment. Third, the thrombus pattern classifications used in this study were based on the dominant patterns of three common components. However, other components, such as the von Willebrand factor, leukocytes, and neutrophil extracellular trap, may also play important roles in the long-term prognosis.[26] Fourth, while we applied a ≥70% dominance rule supplemented by immunohistochemical stain, pattern classification was not fully automated and still involved qualitative judgment. Accordingly, borderline cases such as those between mixed and layered may have been misclassified despite the high inter-rater agreement (κ=0.88). Lastly, although participating tertiary centers followed guideline-concordant secondary prevention pathways, medication exposure was defined at discharge only. We lacked longitudinal data on adherence, dose changes or switching, and warfarin time-in-therapeutic range, and we did not systematically capture rehabilitation intensity or access. These factors importantly influence long-term outcomes, and the lack of data may confound observed associations.

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Conclusions

Our study provides a detailed analysis of thrombus patterns in stroke-causing thrombi, demonstrating that the diffuse platelet pattern is independently associated with a higher risk of MACE, irrespective of comorbidities. Our data indicate that in thrombus research, including the prediction of prognosis, histological distribution patterns may be more important than simple composition. Improving stroke prognosis may require tailored treatment strategies based on the histological features of thrombi.

Supplementary materials

Supplementary materials related to this article can be found online at https://doi.org/10.5853/jos.2025.03412.

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Conflicts of interest

The authors have no financial conflicts of interest.

Author contribution

Conceptualization: Hyungwoo Lee, Young Dae Kim. Study design: Hyungwoo Lee, Young Dae Kim. Methodology: Hyungwoo Lee, Young Dae Kim. Data collection: all authors. Investigation: Young Dae Kim, Hyungwoo Lee. Statistical analysis: Hyungwoo Lee, Young Dae Kim. Writing—original draft: Hyungwoo Lee, Young Dae Kim. Writing—review & editing: Hyungwoo Lee, Hyo Suk Nam, Ji Hoe Heo, Young Dae Kim. Funding acquisition: Young Dae Kim. Approval of final manuscript: all authors.

References

1. Jolugbo P, Ariëns RAS. Thrombus composition and efficacy of thrombolysis and thrombectomy in acute ischemic stroke. *Stroke* 2021;52:1131-1142.
2. Park H, Kim J, Ha J, Hwang IG, Song TJ, Yoo J, et al. Histological features of intracranial thrombi in stroke patients with cancer. *Ann Neurol* 2019;86:143-149.
3. Baek JH, Kwon I, Kim S, Nam HS, Kim YD, Kim BM, et al. Thrombi with a higher erythrocyte composition are more fragile in acute stroke. *J Stroke* 2024;26:454-457.
4. Heo JH, Nam HS, Kim YD, Choi JK, Kim BM, Kim DJ, et al. Pathophysiologic and therapeutic perspectives based on thrombus histology in stroke. *J Stroke* 2020;22:64-75.
5. Staessens S, François O, Brinjikji W, Doyle KM, Vanacker P, Andersson T, et al. Studying stroke thrombus composition after thrombectomy: what can we learn? *Stroke* 2021;52:3718-3727.
6. Shimizu H, Hatakeyama K, Saito K, Shobatake R, Takahashi N, Deguchi J, et al. Age and composition of the thrombus retrieved by mechanical thrombectomy from patients with acute ischemic stroke are associated with revascularization and clinical outcomes. *Thromb Res* 2022;219:60-69.
7. Zhang X, Fu X, Ren Z, Zhou X, Ma Q. Relationship between thrombus composition and prognosis in patients with acute ischemic stroke undergoing mechanical thrombectomy. *J Clin Neurosci* 2024;126:46-51.
8. Heo J, Lee H, Seog Y, Kim S, Baek JH, Park H, et al. Cancer prediction with machine learning of thrombi from thrombectomy in stroke: multicenter development and validation. *Stroke* 2023;54:2105-2113.
9. Heo J, Seog Y, Lee H, Lee IH, Kim S, Baek JH, et al. Automated composition analysis of thrombus from endovascular treatment in acute ischemic stroke using computer vision. *J Stroke* 2022;24:433-435.
10. Marder VJ, Chute DJ, Starkman S, Abolian AM, Kidwell C, Liebeskind D, et al. Analysis of thrombi retrieved from cerebral arteries of patients with acute ischemic stroke. *Stroke* 2006;37:2086-2093.
11. Schuhmann MK, Gunreben I, Kleinschnitz C, Kraft P. Immunohistochemical analysis of cerebral thrombi retrieved by mechanical thrombectomy from patients with acute ischemic stroke. *Int J Mol Sci* 2016;17:298.
12. Weisscher N, Vermeulen M, Roos YB, de Haan RJ. What should be defined as good outcome in stroke trials; a modified Rankin score of 0-1 or 0-2? *J Neurol* 2008;255:867-874.
13. Adams HP Jr, Bendixen BH, Kappelle LJ, Biller J, Love BB, Gordon DL, et al. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of Org 10172 in Acute Stroke Treatment. *Stroke* 1993;24:35-41.
14. Chen Y, Wright N, Guo Y, Turnbull I, Kartsonaki C, Yang L, et al. Mortality and recurrent vascular events after first incident stroke: a 9-year community-based study of 0·5 million Chinese adults. *Lancet Glob Health* 2020;8:e580-e590.
15. Zhang R, Wang Y, Fang J, Yu M, Wang Y, Liu G. Worldwide 1-month case fatality of ischaemic stroke and the temporal trend. *Stroke Vasc Neurol* 2020;5:e000371.

16. Sujijantarat N, Templeton KA, Antonios JP, Renedo D, Koo AB, Haynes JO, et al. Is clot composition associated with cause of stroke? A systematic review and meta-analysis. *Stroke Vasc Interv Neurol* 2024;4:e001426.
17. Rossi R, Fitzgerald S, Molina S, Mereuta OM, Douglas A, Pandit A, et al. The administration of rtPA before mechanical thrombectomy in acute ischemic stroke patients is associated with a significant reduction of the retrieved clot area but it does not influence revascularization outcome. *J Thromb Thrombolysis* 2021;51:545-551.
18. Ahn SH, Hong R, Choo IS, Heo JH, Nam HS, Kang HG, et al. Histologic features of acute thrombi retrieved from stroke patients during mechanical reperfusion therapy. *Int J Stroke* 2016;11:1036-1044.
19. Lee KB, Kim TH, Park J, Park JK, Kang KW, Kim J, et al. Stroke and systemic thromboembolism according to CHA_2DS_2-VASc score in contemporary Korean patients with atrial fibrillation. *Yonsei Med J* 2022;63:317-324.
20. Ospel JM, Brown S, Kappelhof M, van Zwam W, Jovin T, Roy D, et al. Comparing the prognostic impact of age and baseline National Institutes of Health Stroke Scale in acute stroke due to large vessel occlusion. *Stroke* 2021;52:2839-2845.
21. Di Meglio L, Desilles JP, Ollivier V, Nomenjanahary MS, Di Meglio S, Deschildre C, et al. Acute ischemic stroke thrombi have an outer shell that impairs fibrinolysis. *Neurology* 2019;93:e1686-e1698.
22. Cines DB, Lebedeva T, Nagaswami C, Hayes V, Massefski W, Litvinov RI, et al. Clot contraction: compression of erythrocytes into tightly packed polyhedra and redistribution of platelets and fibrin. *Blood* 2014;123:1596-1603.
23. Johnson S, Chueh J, Gounis MJ, McCarthy R, McGarry JP, McHugh PE, et al. Mechanical behavior of in vitro blood clots and the implications for acute ischemic stroke treatment. *J Neurointerv Surg* 2020;12:853-857.
24. Staessens S, De Meyer SF. Thrombus heterogeneity in ischemic stroke. *Platelets* 2021;32:331-339.
25. Staessens S, Denorme F, Francois O, Desender L, Dewaele T, Vanacker P, et al. Structural analysis of ischemic stroke thrombi: histological indications for therapy resistance. *Haematologica* 2020;105:498-507.
26. Cha MJ, Ha J, Lee H, Kwon I, Kim S, Kim YD, et al. Neutrophil recruitment in arterial thrombus and characteristics of stroke patients with neutrophil-rich thrombus. *Yonsei Med J* 2022;63:1016-1026.

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Supplementary Table 1. Univariable cox regression of MACE occurrence

	HR (95% CI)	*P*
Age*		
1st quartile	Reference	
2nd quartile	1.20 (0.95–1.52)	0.132
3rd quartile	1.66 (1.08–2.56)	0.021
4th quartile	2.90 (1.90–4.42)	<0.001
Male sex	0.71 (0.52–0.97)	0.031
Hypertension	1.42 (0.99–2.05)	0.056
Diabetes mellitus	1.35 (0.98–1.87)	0.069
Dyslipidemia	0.85 (0.61–1.18)	0.329
CAOD	1.33 (0.91–1.95)	0.145
PAOD	0.44 (0.11–1.76)	0.245
Atrial fibrillation	1.28 (0.94–1.75)	0.119
Active cancer	4.23 (2.75–6.52)	<0.001
ESRD	3.45 (1.52–7.83)	0.003
Hemoglobin (g/L)	0.99 (0.98–0.99)	<0.001
White blood cell (10^9/L)	1.00 (0.96–1.04)	0.942
Platelet (10^9/L)	1.00 (1.00–1.00)	0.405
C-reactive protein (mg/L)†	1.23 (1.07–1.41)	0.003
D-dimer (nmol/L)†	1.70 (1.46–1.97)	<0.001
Albumin (g/L)	0.97 (0.94–1.01)	0.108
Initial glucose (mmol/L)†	1.97 (1.10–3.53)	0.023
Premorbid disability	2.41 (1.76–3.30)	<0.001
Initial NIHSS	1.04 (1.01–1.06)	0.004
IV tPA	0.73 (0.53–1.01)	0.058
Stroke classification		
Cardioembolism	Reference	
LAA	0.80 (0.50–1.27)	0.346
Other	1.20 (0.85–1.69)	0.303
Onset to recanalization (hr)	1.03 (1.00–1.05)	0.042
Modified TICI ≥2b	0.41 (0.25–0.68)	<0.001
Discharge medication		
None	Reference	
Anticoagulant	0.53 (0.32–0.87)	0.013
Antiplatelet	0.45 (0.26–0.77)	0.004
Both	0.41 (0.19–0.87)	0.020
Platelet (%)	1.02 (1.01–1.03)	0.003
Red blood cell (%)	0.99 (0.98–1.00)	0.020
Fibrin (%)	1.00 (0.99–1.01)	0.300
Pattern		
Layered	Reference	
Erythrocytic	1.34 (0.88–2.02)	0.170
Mixed	1.58 (1.05–2.36)	0.026
Diffuse platelet	3.80 (2.37–6.10)	<0.001

For continuous variables, HRs represent the effect per one-unit increase in the variable. For log-transformed variables, HRs represent the effect per one-unit increase in the natural log-transformed value.
MACE, major adverse cardiovascular events; HR, hazard ratio; CI, confidence interval; CAOD, coronary artery occlusive disease; PAOD, peripheral artery occlusive disease; ESRD, end stage renal disease; NIHSS, National Institutes of Health Stroke Scale; tPA, tissue plasminogen activator; LAA, large artery atherosclerosis; TICI, Thrombolysis in Cerebral Infarction.
*Age was modeled with restricted cubic splines (four knots); †Natural log-transformed.

Supplementary Table 2. Multivariable-adjusted* analysis of MACE based on immunohistochemical staining patterns

	HR (95% CI)	*P*
Pattern		
Layered	Reference	
Erythrocytic	1.23 (0.73–2.08)	0.436
Mixed	1.44 (0.87–2.37)	0.152
Diffuse platelet	2.35 (1.11–4.98)	0.026
Age†	1.03 (1.01–1.05)	
1st quartile	Reference	
2nd quartile	1.05 (0.72–1.42)	0.726
3rd quartile	1.35 (0.76–2.38)	0.305
4th quartile	2.25 (1.23–4.12)	0.008
Male sex	1.07 (0.71–1.61)	0.748
Active cancer	2.41 (1.20–4.82)	0.013
ESRD	1.70 (0.59–4.88)	0.321
Premorbid disability	1.56 (0.99–2.45)	0.051
Hemoglobin (g/L)	1.00 (0.99–1.01)	0.709
C-reactive protein (mg/L)‡	1.00 (0.85–1.19)	0.963
D-dimer (nmol/L)‡	1.42 (1.15–1.76)	0.001
Initial glucose (mmol/L)‡	1.63 (0.80–3.30)	0.177
Initial NIHSS	1.03 (1.00–1.07)	0.050
Onset to recanalization (hr)	1.03 (1.00–1.06)	0.024
Modified TICI ≥2b	0.38 (0.21–0.68)	<0.001
Discharge medication		
None	Reference	
Anticoagulant	0.83 (0.40–1.74)	0.625
Antiplatelet	0.74 (0.34–1.63)	0.453
Both	0.72 (0.27–1.93)	0.512
Platelet (%)	0.99 (0.98–1.01)	0.529
Red blood cell (%)	1.00 (0.99–1.01)	0.795

For continuous variables, HRs represent the effect per one-unit increase. For log-transformed variables, HRs represent the effect per one-unit increase in the natural log-transformed value.
MACE, major adverse cardiovascular events; HR, hazard ratio; CI, confidence interval; ESRD, end stage renal disease; NIHSS, National Institutes of Health Stroke Scale; TICI, Thrombolysis in Cerebral Infarction.
*Adjusted for age (restricted cubic splines, four knots), sex, active cancer, ESRD, poor premorbid status, natural log-transformed biomarkers (C-reactive protein, D-dimer, initial glucose), initial NIHSS, onset to recanalization time, immediate modified TICI, discharge medication, platelet staining, and red blood cell staining; †Age was modeled with restricted cubic splines (four knots). For presentation, HRs are shown for age quartiles (Q2–Q4 vs. Q1), evaluated at the within-quartile medians and derived from the spline model using contrasts; ‡Natural log-transformed.

Supplementary Table 3. Sensitivity analyses for stroke and IHD: Firth-penalized Cox models with minimal adjustment

Outcome	Pattern	HR (95% CI)	*P*
Stroke*			
	Layered	Reference	
	Erythrocytic	1.94 (1.00–3.81)	0.050
	Mixed	1.92 (0.95–3.86)	0.067
	Diffuse platelet	6.31 (2.74–14.08)	<0.001
IHD†			
	Layered	Reference	
	Erythrocytic	1.59 (0.41–6.19)	0.490
	Mixed	1.22 (0.27–5.04)	0.777
	Diffuse platelet	0.48 (0.01–4.62)	0.586

HR, hazard ratio; CI, confidence interval; IHD, ischemic heart disease.
*Adjusted for age, sex, active cancer, and initial National Institutes of Health Stroke Scale; †Adjusted for age and sex.

Supplementary Table 4. Sensitivity analysis including patients who died within 4 weeks after the index event

Outcome	Pattern	HR (95% CI)	*P*
MACE			
	Layered	Reference	
	Erythrocytic	1.17 (0.71–1.93)	0.530
	Mixed	1.35 (0.83–2.19)	0.217
	Diffuse platelet	2.30 (1.14–4.67)	0.021
All-cause death			
	Layered	Reference	
	Erythrocytic	0.90 (0.48–1.69)	0.750
	Mixed	1.39 (0.76–2.55)	0.290
	Diffuse platelet	3.47 (1.49–8.07)	0.004
Stroke			
	Layered	Reference	
	Erythrocytic	1.87 (0.76–4.58)	0.173
	Mixed	1.57 (0.63–3.88)	0.333
	Diffuse platelet	5.57 (1.58–19.61)	0.008
IHD			
	Layered	Reference	
	Erythrocytic	2.93 (0.28–30.29)	0.368
	Mixed	0.88 (0.06–11.48)	0.919
	Diffuse platelet	N/A	N/A

HR, hazard ratio; CI, confidence interval; MACE, major adverse cardiovascular events; IHD, ischemic heart disease; N/A, not applicable.
*Adjusted for age (restricted cubic splines, four knots), sex, active cancer, end stage renal disease, poor premorbid status, natural log-transformed biomarkers (C-reactive protein, D-dimer, initial glucose), initial National Institutes of Health Stroke Scale, onset to recanalization time, immediate modified Thrombolysis in Cerebral Infarction, discharge medication, platelet staining, and red blood cell staining.

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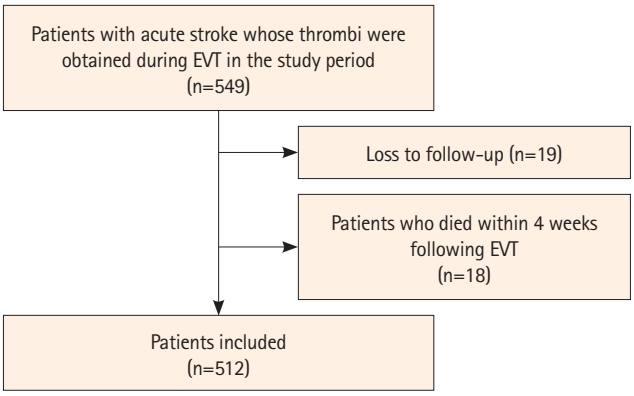
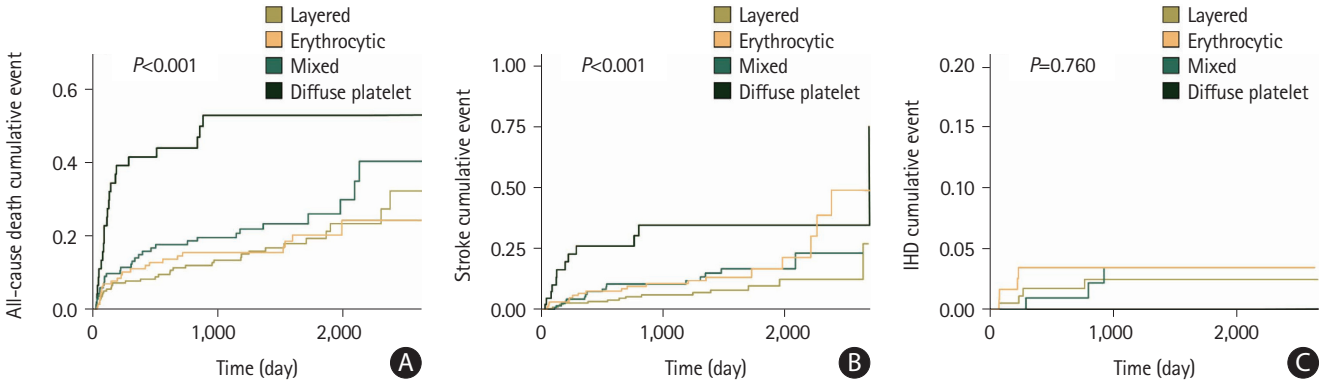
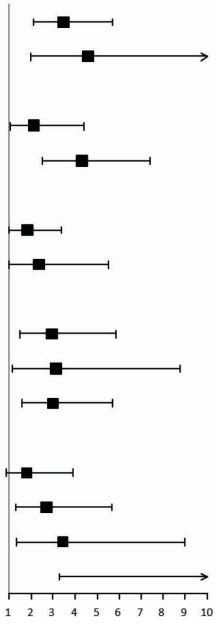


Supplementary Figure 1. Patient flow diagram. EVT, endovascular thrombectomy.

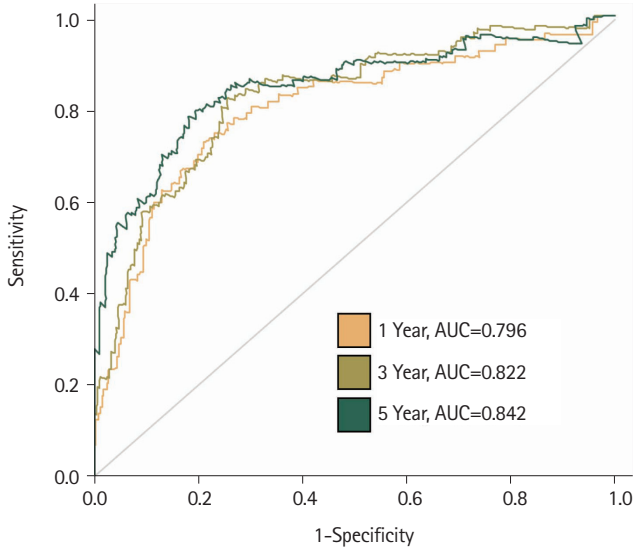


Supplementary Figure 2. Cumulative Incidence of cardiovascular outcome by immunohistochemical staining patterns. (A) All-cause death. (B) Stroke. (C) Ischemic heart disease (IHD).

Subgroup	N	HR (95% CI)	P for interaction
Age			0.589
Over 65	380	3.45 (2.10-5.69)	
Under 65	132	4.57 (1.98-10.56)	
Atrial fibrillation			0.098
Yes	272	2.11 (1.02-4.38)	
No	240	4.28 (2.48-7.38)	
Active cancer			0.511
Yes	37	1.80 (0.97-3.35)	
No	475	2.33 (0.98-5.52)	
TOAST classification			0.837
CE	296	2.94 (1.47-5.85)	
LAA	83	3.13 (1.12-8.74)	
Other	133	2.97 (1.55-5.72)	
Discharge medication			0.522
Anticoagulant	270	1.79 (0.82-3.92)	
Antiplatelet	160	2.69 (1.28-5.65)	
None	38	3.44 (1.31-8.99)	
Both	44	12.75 (3.28-49.59)	



Supplementary Figure 3. Subgroup analysis of the impact of diffuse platelet pattern on the occurrence of major adverse cardiovascular events. HR, hazard ratio; CI, confidence interval; TOAST, Trial of Org 10172 in Acute Stroke Treatment; CE, cardioembolism; LAA, large artery atherosclerosis.



Supplementary Figure 4. ROC curve of the multivariable cox regression model for predicting major adverse cardiovascular events. ROC, receiver operating characteristic; AUC, area under the curve.

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