RESEARCH ARTICLE

Early prediction of severity in acute ischemic stroke and transient ischemic attack using platelet parameters and neutrophil-to-lymphocyte ratio

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Background: It is still not easy to predict severity promptly in patients with acute ischemic stroke (AIS) and transient ischemic attack (TIA). We investigated that platelet parameters or combinations of them could be a useful tool for early prediction of severity of AIS and TIA at admission and after 3 months.

Methods: We prospectively recruited 104 patients newly diagnosed with AIS and TIA. We investigated their neutrophil-to-lymphocyte ratio (NLR) and platelet parameters. According to the Modified Rankin Scale scores, the patients were divided into two groups.

Results: In receiver operating characteristic (ROC) curve analyses, mean platelet volume (MPV), NLR/platelet count (PLT), MPV/PLT, MPV*NLR, and MPV*NLR/PLT showed statistically significant results in both at admission and after 3 months. Values of area under ROC curves for those tests at admission were 0.646, 0.697, 0.664, 0.708, and 0.722, respectively. Also, values after 3 months were 0.591, 0.661, 0.638, 0.662, and 0.689, respectively.

Conclusion: MPV*NLR/PLT could be used as a relatively good tool for predicting severity at the time of admission and after 3 months than other parameters or combinations of them. Further studies have to be carried out to investigate the best parameter for predicting the severity of AIS and TIA.

KEYWORDS

acute ischemic stroke, mean platelet volume, neutrophil-to-lymphocyte ratio, platelet count, platelet parameter, transient ischemic attack

1 | INTRODUCTION

Platelets have a central role in normal hemostatic process, as well as abnormal conditions, bleeding, and thrombosis.¹ Recently, it has been known that excessive hyperactivity of platelets increases the risk of thromboembolism, leading to excessive formation of abnormal thrombosis together with atherosclerotic lesion, and is a major factor in causing acute ischemic stroke (AIS).² The interaction between platelets and vascular endothelial cells could induce local inflammatory conditions in the blood vessels, leading to microcirculatory

disturbances so that these conditions promote the progression to atherosclerosis gradually.³⁻⁶

Since the use of antiplatelet agents was reported to be effective in the prevention and treatment of various cardiocerebrovascular diseases,⁷ there has been a growing interest in the role of platelets in the development of cardiocerebrovascular diseases. Although there have been many studies on the role of platelets in various clinical risk factors, cell-cell interactions, and pathogenesis of thrombo-inflammatory diseases, availability and limitation of the platelet parameters that could be applied to an actual clinical setting are not

well known. Most clinical studies in Korea have been limited to the improvement of treatment results related to drugs and procedures.

A recent hematology analyzer is a fully automated system so that it can test the complete blood cell count (CBC), differential leukocyte count, and platelet parameters including platelet count (PLT), mean platelet volume (MPV), platelet distribution width (PDW), and plateletcrit (PCT) within a short time and report a large amount of information quickly. Because they are the most basic and relatively inexpensive diagnostic tests, these tests are performed not only for distinguishing the causes of hematologic diseases such as anemia, leukocyte diseases, and platelet-related diseases, but for suspected AIS patients routinely.

In this study, we aimed to evaluate whether these parameters or combinations of them could be a useful tool for early prediction of severity of AIS and transient ischemic attack (TIA) at admission and after 3 months.

2 | MATERIALS AND METHODS

2.1 | Study population

We prospectively recruited 104 adult patients who were newly diagnosed with AIS and TIA between July 2015 and May 2017 at Cerebrovascular Center of Dong-A University Hospital. The patients were recruited according to their first diagnoses of AIS and TIA, which were based on their symptoms, physical and neurologic examination, and brain CT or MRI findings. The patients with any evidences of infection, inflammation, hematologic disease, or malignancy were excluded from the study population. The consents from patients were exempted because we used their residual blood samples without any additional blood samplings. We investigated their baseline characteristics including sex, age, past histories, underlying diseases, and social histories. Stroke etiology was classified as follows: large-artery atherosclerosis, cardioembolism, small-artery occlusion, and other determined or undetermined. Clinical data were assessed by their electronic medical records.

The severity of AIS and TIA was estimated at admission and after 3 months using the Modified Rankin Scale (MRS)⁸ which scores patients from 0 (asymptomatic) to 6 (dead). According to the MRS scores, the patients were divided into two groups: good consequence group for scores 0 to 2 and poor consequence group for scores 3 to 6. We investigated whether there were statistically significant differences in blood parameters between the two groups, and then, we evaluated which combinations of those parameters could be useful for early prediction of severity of AIS and TIA at admission and after 3 months.

2.2 | Blood tests

Blood samples were immediately taken from the patients within 3 hours after the onset of disease, and blood tests were performed within 30 minutes after they arrived at our hospital. Results of CBC,

differential leukocyte count, and platelet parameters including PLT, MPV, PDW, and PCT were obtained using the Cell-Dyn Sapphire automated hematology analyzer (Abbott Diagnostics, Santa Clara, CA, USA) according to the manufacturer's instructions. The test was performed within 30 minutes of blood sampling. The analyzer was calibrated regularly, and internal quality control was performed once daily using tri-level control materials.

2.3 | Statistical analyses

Statistical analysis was performed using MedCalc for Windows, version 12.7.0.0 (MedCalc Software, Mariakerke, Belgium). *P*-values of <0.05 were regarded as significant. Chi-square test was used for comparison of categorical data, and chi-square test for trend method was used for comparison of three or more groups. Independent *t* test and Mann-Whitney *U* test were used to compare continuous variables between the two groups. The results were expressed as numbers with percentages for categorical variables or mean $\pm$ standard deviation for measurement data.

Multivariate analysis was performed by multiple logistic regression analysis for adjustment of confounding factors. For multivariate analysis, we included variables with a *P*-value of <0.2 in univariate analysis. We replaced blood parameters with dummy variables based on the interquartile range (IQR) and investigated parameters showing statistically significant results. Results were presented as 95% confidence interval with odds ratio.

Receiver operating characteristic (ROC) curve analysis was performed for parameters to determine the sensitivity and specificity according to the cutoff value. Area under ROC curve (AUC) was used to evaluate the performance of parameters and combinations of them for discriminating two groups.

3 | RESULTS

3.1 | Basic characteristics of the study population

Of the 104 patients, 41 had MRS scores of 2 or less (good consequence group) and 63 had scores of 3 or more (poor consequence group) at admission. Based on the scores after 3 months, 56 were good consequence group and 36 were poor consequence group. The other 12 patients were excluded for follow-up <3 months. The baseline characteristics of the two groups based on the MRS scores in the study population were summarized in Table 1. There were no statistically significant differences between the two groups in baseline characteristics including sex, underlying diseases (hypertension, diabetes, and dyslipidemia), past history of coronary artery diseases and atrial fibrillation, current smoking, and stroke etiology, except for age distribution. The mean age of the good consequence group at admission was statistically significantly lower than that of the poor consequence group ($P = 0.046$). After 3 months, the difference in age distribution was similar, but not statistically significant ($P = 0.055$).

TABLE 1 Baseline characteristics according to MRS score at admission and after 3 mo

Variable	MRS-0 scores ≤ 2 (N = 41)	MRS-0 scores ≥ 3 (N = 63)	P	MRS-3 M scores ≤ 2 (N = 56)	MRS-3 M scores ≥ 3 (N = 36)	P
Male, N (%)	25 (61.0)	34 (54.0)	0.615	37 (66.1)	17 (47.2)	0.075
Age (years)	64.83 $\pm$ 13.43	69.63 $\pm$ 10.75	0.046	65.32 $\pm$ 12.00	70.11 $\pm$ 10.83	0.055
Hypertension, N (%)	28 (68.3)	44 (69.8)	0.960	38 (67.9)	26 (72.2)	0.659
Diabetes, N (%)	13 (31.7)	19 (30.2)	0.960	19 (33.9)	12 (33.3)	0.953
Dyslipidemia, N (%)	8 (19.5)	6 (9.5)	0.244	8 (14.3)	5 (13.9)	0.958
Coronary artery disease, N (%)	5 (12.2)	8 (12.7)	0.820	6 (10.7)	5 (13.9)	0.649
Atrial fibrillation, N (%)	5 (12.2)	15 (23.8)	0.225	7 (12.5)	8 (22.2)	0.221
Current smoking, N (%)	10 (24.4)	15 (23.8)	0.867	15 (26.8)	7 (19.4)	0.423
Etiology, N (%)						
Large-artery atherosclerosis	13 (31.7)	18 (28.6)	0.201	16 (28.6)	11 (30.6)	0.258
Cardioembolism	2 (4.9)	15 (23.8)		4 (7.1)	8 (22.2)	
Small-artery occlusion	4 (9.8)	9 (14.3)		9 (16.1)	4 (11.1)	
Other determined or undetermined	22 (53.7)	21 (33.3)		27 (48.2)	13 (36.1)	

MRS-0, modified Rankin Scale score at admission; MRS-3 M, modified Rankin Scale score after 3 mo.

3.2 | Statistical comparisons of the good consequence group and the poor consequence group

The results of comparing two groups with blood parameters at admission and after 3 months were summarized in Table 2. At the time of admission, there were no statistically significant differences in red cell count, hemoglobin, hematocrit, WBC, PDW, and PCT between the two groups. WBC in the poor consequence

group was higher than that in the good consequence group, but not statistically significant ($P = 0.068$). There was a significant difference in neutrophil-to-lymphocyte ratio (NLR), PLT, and MPV between the two groups at admission ($P = 0.002$, 0.044 , and 0.009 , respectively). NLR and MPV were higher in poor consequence group, and PLT was lower in good consequence group. In addition, there was no statistically significant difference in C-reactive protein (CRP) levels between the two groups ($P = 0.340$).

TABLE 2 Comparison of blood parameters according to MRS score at admission and after 3 mo

Parameter	MRS-0 scores ≤ 2 (N = 41)	MRS-0 scores ≥ 3 (N = 63)	P	MRS-3 M scores ≤ 2 (N = 56)	MRS-3 M scores ≥ 3 (N = 36)	P
Red cell count ($\times 10^{12}/L$)	4.44 $\pm$ 0.62	4.48 $\pm$ 0.56	0.780 ^a	4.52 $\pm$ 0.60	4.47 $\pm$ 0.50	0.627 ^a
Hemoglobin (g/dL)	13.84 $\pm$ 1.96	14.02 $\pm$ 1.67	0.604 ^a	14.11 $\pm$ 1.76	14.04 $\pm$ 1.65	0.869 ^a
Hematocrit (%)	39.78 $\pm$ 5.65	40.64 $\pm$ 4.97	0.416 ^a	40.66 $\pm$ 5.16	40.66 $\pm$ 4.82	0.996 ^a
White cell count ($\times 10^9/L$)	7.81 $\pm$ 1.80	8.69 $\pm$ 3.05	0.068 ^a	8.20 $\pm$ 2.77	8.70 $\pm$ 2.73	0.291 ^b
NLR	2.38 $\pm$ 1.71	4.41 $\pm$ 4.22	0.002 ^b	2.92 $\pm$ 2.63	4.08 $\pm$ 2.79	0.033 ^b
Platelet count ($\times 10^9/L$)	260.12 $\pm$ 75.35	232.58 $\pm$ 61.63	0.044 ^a	254.96 $\pm$ 77.02	231.19 $\pm$ 56.42	0.114 ^a
MPV (fL)	8.18 $\pm$ 1.06	8.84 $\pm$ 1.33	0.009 ^a	8.45 $\pm$ 1.42	8.77 $\pm$ 0.96	0.142 ^b
PDW (%)	15.26 $\pm$ 1.85	15.07 $\pm$ 2.15	0.939 ^b	15.24 $\pm$ 1.90	15.31 $\pm$ 1.96	0.444 ^b
PCT (%)	0.220 $\pm$ 0.062	0.205 $\pm$ 0.054	0.224 ^a	0.217 $\pm$ 0.064	0.204 $\pm$ 0.050	0.308 ^a
NLR/PLT	0.010 $\pm$ 0.008	0.022 $\pm$ 0.034	0.001 ^b	0.013 $\pm$ 0.014	0.018 $\pm$ 0.013	0.009 ^b
MPV/PLT	0.035 $\pm$ 0.015	0.042 $\pm$ 0.023	0.005 ^b	0.038 $\pm$ 0.025	0.040 $\pm$ 0.011	0.026 ^b
MPV*NLR	19.08 $\pm$ 11.91	39.08 $\pm$ 42.56	<0.001 ^b	24.51 $\pm$ 24.32	34.50 $\pm$ 22.03	0.009 ^b
MPV*NLR/PLT	0.080 $\pm$ 0.058	0.205 $\pm$ 0.354	<0.001 ^b	0.112 $\pm$ 0.141	0.155 $\pm$ 0.108	0.002 ^b

MPV, mean platelet volume; MRS-0, modified Rankin Scale score at admission; MRS-3 M, modified Rankin Scale score after 3 mo; NLR, neutrophil-to-lymphocyte ratio; PCT, plateletcrit; PDW, platelet distribution width.

^aComparisons by Independent t test.

^bComparisons by Mann-Whitney U test.

After 3 months, tendencies of NLR, PLT, and MPV were similar to those at the time of admission between the two groups, but there was a statistically significant difference only in NLR ($P = 0.033$). On the other hand, there was no statistically significant difference in PLT and MPV ($P = 0.114$ and 0.142 , respectively).

Values of NLR/PLT, MPV/PLT, MPV*NLR, and MPV*NLR/PLT were obtained by combining NLR, PLT, and MPV. These

combined values were also used to compare between the two groups, and all of them showed statistically significant differences at admission ($P = 0.001$, 0.005 , <0.001 , and <0.001 , respectively) and after 3 months ($P = 0.009$, 0.026 , 0.009 , and 0.002 , respectively).

For the multiple logistic regression analysis, each value of WBC, NLR, PLT, MPV, NLR/PLT, MPV/PLT, MPV*NLR, and MPV*NLR/

TABLE 3 Association of age and parameters with the severity of AIS and TIA at admission by multivariate logistic regression analysis

Variable	Univariate		Multivariate	
	OR (95% CI)	P	OR (95% CI)	P
Age (years)				
<59	1.00		1.00	
60-69	2.94 (0.97-8.90)	0.056	3.21 (0.92-11.18)	0.067
70-79	2.92 (1.01-8.45)	0.049	2.85 (0.88-9.25)	0.080
>80	1.96 (0.48-7.99)	0.348	2.04 (0.43-9.56)	0.367
White cell count ($\times 10^9/L$)				
<6.645	1.00		1.00	
6.645-9.495	1.60 (0.62-4.14)	0.332	2.29 (0.77-6.84)	0.137
>9.495	2.25 (0.72-6.99)	0.161	4.43 (1.14-17.19)	0.032
NLR				
<1.5878	1.00		1.00	
1.5878-4.0506	1.86 (0.72-4.8)	0.202	1.79 (0.62-5.18)	0.279
>4.0506	7.50 (2.01-28.05)	0.003	9.69 (2.31-40.62)	0.002
Platelet count ($\times 10^9/L$)				
<199.0	1.00		1.00	
199.0-285.5	0.77 (0.28-2.11)	0.614	1.34 (0.41-4.43)	0.626
>285.5	0.38 (0.12-1.19)	0.096	0.77 (0.20-3.01)	0.712
MPV (fL)				
<7.700	1.00		1.00	
7.700-9.235	2.10 (0.80-5.51)	0.132	2.75 (0.86-8.76)	0.087
>9.235	3.45 (1.07-11.16)	0.038	4.46 (1.13-17.61)	0.033
NLR/PLT				
<0.007114	1.00		1.00	
0.007114-0.01802	2.36 (0.90-6.20)	0.081	2.33 (0.82-6.62)	0.112
>0.01802	8.80 (2.34-33.15)	0.001	9.12 (2.26-36.82)	0.002
MPV/PLT				
<0.02885	1.00		1.00	
0.02885-0.04624	1.59 (0.62-4.10)	0.337	1.91 (0.66-5.51)	0.232
>0.04624	4.90 (1.41-16.99)	0.012	5.15 (1.31-20.24)	0.019
MPV*NLR				
<14.0925	1.00		1.00	
14.0925-35.3835	2.56 (0.97-6.74)	0.057	2.30 (0.81-6.53)	0.118
>35.3835	6.72 (1.92-23.58)	0.003	7.79 (2.03-29.92)	0.003
MPV*NLR/PLT				
<0.05791	1.00		1.00	
0.05791-0.1523	4.25 (1.55-11.67)	0.005	3.55 (1.24-10.15)	0.018
>0.1523	9.45 (2.62-34.07)	<0.001	8.73 (2.32-32.80)	0.001

AIS, acute ischemic stroke; CI, confidence interval; MPV, mean platelet volume; NLR, neutrophil-to-lymphocyte ratio; OR, odds ratio; PLT, platelet count; TIA, transient ischemic attack.

PLT was converted to dummy variables based on their IQR. At admission, WBC, NLR, MPV, NLR/PLT, MPV/PLT, and MPV*NLR had significantly high odds ratios in the range above third quartile (Q3), and MPV*NLR/PLT showed significantly high odds ratios in both their IQR and range above Q3. On the other hand, after 3 months, MPV had significantly high odds ratio in its IQR, and MPV/PLT and MPV*NLR had significantly high odds ratio in their range above Q3. NLR/PLT and MPV*NLR/PLT had significantly high odds ratio in

both their IQR and range above Q3. The results of the univariate and multivariate analyses were summarized with their specific odds ratios and *P*-values in Tables 3 and 4.

3.3 | The ROC curve analyses

In the ROC curve analyses, AUC values were calculated using parameters that showed statistically significant results in both at admission

TABLE 4 Association of sex, age, and parameters with the severity of AIS and TIA after 3 mo by multivariate logistic regression analysis

Variable	Univariate		Multivariate	
	OR (95% CI)	<i>P</i>	OR (95% CI)	<i>P</i>
Male, N (%)				
Female	1.00		1.00	
Male	0.46 (0.20-1.08)	0.075	0.42 (0.15-1.22)	0.110
Age (years)				
<59	1.00		1.00	
60-69	1.67 (0.50-5.51)	0.402	2.08 (0.50-8.58)	0.313
70-79	1.75 (0.54-5.62)	0.347	1.36 (0.34-5.53)	0.665
>80	3.33 (0.57-19.59)	0.183	3.22 (0.38-27.35)	0.285
NLR				
<1.5878	1.00		1.00	
1.5878-4.0506	1.00 (0.34-2.98)	0.994	1.21 (0.34-4.28)	0.770
>4.0506	3.33 (0.98-11.37)	0.055	3.93 (0.97-15.97)	0.056
Platelet count ($\times 10^9/L$)				
<199.0	1.00		1.00	
199.0-285.5	0.45 (0.16-1.26)	0.128	0.54 (0.16-1.85)	0.327
>285.5	0.40 (0.12-1.27)	0.121	0.38 (0.87-1.63)	0.192
MPV (fL)				
<7.700	1.00		1.00	
7.700-9.235	4.80 (1.41-16.36)	0.012	5.43 (1.36-21.67)	0.017
>9.235	1.59 (0.38-6.71)	0.525	2.05 (0.40-10.56)	0.392
NLR/PLT				
<0.007114	1.00		1.00	
0.007114-0.01802	3.05 (0.89-10.45)	0.075	4.69 (1.14-19.30)	0.032
>0.01802	7.39 (1.89-28.94)	0.004	9.26 (1.99-43.10)	0.005
MPV/PLT				
<0.02885	1.00		1.00	
0.02885-0.04624	1.67 (0.57-4.86)	0.346	2.08 (0.65-6.64)	0.219
>0.04624	3.21 (0.98-10.45)	0.053	4.76 (1.21-18.67)	0.025
MPV*NLR				
<14.0925	1.00		1.00	
14.0925-35.3835	1.51 (0.50-4.59)	0.466	2.04 (0.57-7.34)	0.275
>35.3835	4.41 (1.26-15.41)	0.020	5.41 (1.36-21.53)	0.017
MPV*NLR/PLT				
<0.05791	1.00		1.00	
0.05791-0.1523	4.30 (1.11-16.58)	0.034	6.67 (1.50-29.66)	0.013
>0.1523	9.85 (2.25-43.18)	0.002	15.41 (3.01-78.91)	0.001

AIS, acute ischemic stroke; CI, confidence interval; MPV, mean platelet volume; NLR, neutrophil-to-lymphocyte ratio; OR, odds ratio; PLT, platelet count; TIA, transient ischemic attack.

and after 3 months, such as MPV, NLR/PLT, MPV/PLT, MPV*NLR, and MPV*NLR/PLT. Values of AUC for MPV, NLR/PLT, MPV/PLT, MPV*NLR, and MPV*NLR/PLT at admission were 0.646, 0.697, 0.664, 0.708, and 0.722, respectively. Also, values of AUC after 3 months were 0.591, 0.661, 0.638, 0.662, and 0.689, respectively. The results of the ROC curve analyses with their AUC and *P*-values were shown in Figure 1 and Table 5.

4 | DISCUSSION

As a disease of the stroke spectrum, TIA had traditionally been defined as a transient loss of neurological function lasting within 24 hours. With the development of diagnostic imaging technologies, it has been redefined with an emphasis on tissue injury: A transient episode of neurological dysfunction caused by focal brain, spinal cord, or retinal ischemia, without acute infarction.⁹ Like AIS patients, most TIA patients visit the emergency room or primary care clinic, and in some cases, it might be difficult to distinguish TIA from AIS at first. In addition, it could be difficult to predict initial and afterward severity of AIS and TIA. Therefore, if there were an objective laboratory tool for risk stratification in an emergency such as AIS or TIA, it would be helpful in many ways.

Of platelet parameters, PLT is a well-known parameter that reflects thrombopoiesis, platelet consumption, and senescence for a constant balance of platelets.¹⁰ PLT and MPV were reported as independent risk factors for AIS.¹¹ MPV, which is the mean volume of platelets, reflects platelet function and activation. Previous studies have found a relation between MPV value and cardiocerebrovascular diseases. MPV value can be elevated in AIS, myocardial infarction, and certain clinical states including diabetes and hypercholesterolemia.¹² MPV value is associated with the severity of AIS so that MPV value could be useful for discriminating severe AIS from mild forms.¹³ Also, increased MPV value is associated with poor prognosis in myocardial infarction or restenosis following coronary angioplasty.^{12,14,15}

On the other hand, NLR is a value that can be calculated simply from differential leukocyte count and is known as an indicator of systemic inflammation.¹⁶ In previous studies, the value of NLR is significantly higher in patients with AIS than in normal group.^{17,18}

Likewise, each value of PLT, MPV, and NLR seems to have a correlation with initial stage of AIS and TIA. Based on the previous

studies that MPV is associated with platelet activation and severity of AIS,^{11,13} and the NLR is significantly higher in AIS,^{17,18} it is possible to deduce that multiplying these values would be helpful to predict severity of the disease. In addition, since the PLT value is an index reflecting the platelet consumption,¹⁰ dividing by the PLT value could increase the discrimination power in prediction of the disease severity.

To our knowledge, there have been few studies investigating the association of values obtained by combination of some parameters with initial and afterward severity of AIS and TIA. Moreover, for this kind of purpose, there have been few studies using the Cell-Dyn Sapphire automated hematology analyzer. It is a fully automated system and is based on the principles of multi-angle polarized scatter separation, focused flow impedance, and flow cytometry.^{19,20} Our findings showed that MPV*NLR/PLT could be used as a relatively good tool for predicting severity at the time of admission and after 3 months than other parameters or combinations of them, such as MPV, NLR/PLT, MPV/PLT, and MPV*NLR.

This study has several limitations as follows. It would be necessary to conduct studies on more patients, because the study population was relatively small. Since the follow-up period was rather short, it would also be meaningful to investigate their MRS scores after one year and compare them with various parameters. There could be a selection bias in this study, because it is only for the patients who visited a tertiary hospital in Korea. The stroke etiology was roughly determined in this study so that it could not reflect the detailed clinical causes. We did not consider their medication histories before the diagnoses of AIS and TIA because of a lack of exact information on them in this study. In addition, because the MRS scoring for patients was not always assigned by the same physician, there could be a little bit of discrepancy in the score depending on the physician.

We evaluated only whether each parameter could be a useful tool for early prediction of severity of AIS and TIA at admission and after 3 months without considering the intergroup movement of each patient. In this study, of the patients who were poor consequence group at admission, 20 patients were changed to good consequence group after 3 months, and conversely, one patient was changed from good consequence group to poor consequence group. Among the patients who did not move between groups, 10 patients had higher MRS scores after 3 months. In additional studies, it may also be helpful to consider changes in MRS scores or intergroup movements after treatment with more patients.

FIGURE 1 Receiver operating characteristic curves for mean platelet volume (MPV), neutrophil-to-lymphocyte ratio (NLR)/platelet count (PLT), MPV/PLT, MPV*NLR, and MPV*NLR/PLT (A) at admission and (B) after 3 mo

TABLE 5 The AUC and P-value of each parameter by the ROC curve analyses

Parameter	AUC (at admission)	P	AUC (after 3 mo)	P
MPV	0.646	0.009	0.591	0.125
NLR/PLT	0.697	<0.001	0.661	0.006
MPV/PLT	0.664	0.003	0.638	0.019
MPV*NLR	0.708	<0.001	0.662	0.006
MPV*NLR/PLT	0.722	<0.001	0.689	0.001

AUC, area under the curve; MPV, mean platelet volume; NLR, neutrophil-to-lymphocyte ratio; PLT, platelet count; ROC, receiver operating characteristic.

According to the indications, treatments with thrombolytic agents could be started immediately for patients newly diagnosed with AIS to reduce stroke-induced disabilities and deaths.^{21,22} Although anticoagulants or antiplatelet agents such as the clopidogrel are administered for the prevention of recurrent events, previous studies have shown that the response to clopidogrel could vary from patient to patient, and clopidogrel may not be effective in a significant number of patients.²³⁻²⁹ It is known that the aspirin has similar but lesser problems with resistance.^{23-25,30} In this study, although there was no statistically significant difference in treatment modalities between the two groups, in some patients, the MRS score was elevated after 3 months. It may be beneficial to perform additional studies on these patients through stepwise approaches by the flow cytometry and genetic studies as well as platelet function testing such as platelet aggregometry.³¹⁻³³

Also, it is necessary to consider many clinical situations that may affect NLR. NLR is clearly known to be associated not only with systemic inflammation but also with various disorders such as diabetes, acute coronary syndrome, cancers, liver cirrhosis, ulcerative colitis, and Alzheimer's disease.³⁴⁻⁴⁰ However, for follow-up period, we could not consistently check their CRP levels, which reflect inflammatory states, and such various clinical situations were not fully taken into account. And if the lymphocyte count is too low for any causes, the NLR value can be surprisingly high. The outlier standard for the lymphocyte count was not specified in this study so that it might be necessary to deal with the outlier when actually applied in a clinical setting.

In summary, our findings showed that there were statistically significant differences in NLR, NLR/PLT, MPV/PLT, MPV*NLR, and MPV*NLR/PLT between the good consequence group and the poor consequence group. Among the parameters, MPV*NLR/PLT could be a relatively better tool for early prediction of severity of AIS and TIA at admission and after 3 months. Further studies have to be carried out to investigate the best parameter for predicting the severity or prognosis of AIS and TIA.

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ETHIC STATEMENT

This study was approved by the institutional review board of Dong-A university hospital. This study used residual samples collected in the course of routine CBC tests, and informed consent was exempted by the board.

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