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National Institutes of Health Stroke Scale Score Less Than 10 at 24 hours After Stroke Onset Is a Strong Predictor of a Favorable Outcome After Mechanical Thrombectomy

Takehiro Katano, MD *
Kentaro Suzuki, MD, PhD*
Masataka Takeuchi, MD‡
Masafumi Morimoto, MD, PhD§
Ryuzaburo Kanazawa, MD, PhD‖
Yohei Takayama, MD¶
Junya Aoki, MD, PhD*
Yasuhiro Nishiyama, MD, PhD*
Toshiaki Otsuka, MD, PhD#
Yuji Matsumaru, MD, PhD**
Kazumi Kimura, MD, PhD*
on behalf of the SKIP study Investigators

*Department of Neurology, Nippon Medical School, Tokyo, Japan; ‡Department of Neurosurgery, Seisho Hospital, Kanagawa, Japan; §Department of Neurosurgery, Yokohama Shintoshi Neurosurgery Hospital, Kanagawa, Japan; ‖Department of Neurosurgery, Nagareyama Central Hospital, Chiba, Japan; ¶Department of Neurology, Akiyama Neurosurgical Hospital, Kanagawa, Japan; #Department of Hygiene and Public Health, Nippon Medical School, Tokyo, Japan; **Division of Stroke Prevention and Treatment, Department of Neurosurgery, Faculty of Medicine, University of Tsukuba, Ibaraki, Japan

Correspondence:
Takehiro Katano, MD,
Department of Neurology,
Nippon Medical School,
1-1-5, Sendagi, Bunkyo-ku,
Tokyo 113-8602, Japan.
Email: t-katano@nms.ac.jp

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BACKGROUND: There are a few accurate predictors of patient outcomes after mechanical thrombectomy (MT).

OBJECTIVE: To investigate whether the National Institutes of Health Stroke Scale (NIHSS) score 24 hours after stroke onset could predict favorable outcomes at 90 days in patients with acute stroke treated with MT.

METHODS: Patients from the SKIP study were enrolled in this study. Using receiver operating characteristic curves, the optimal cut-off NIHSS score 24 hours after stroke onset was calculated to distinguish between favorable (modified Rankin Scale score 0-2) and unfavorable (modified Rankin Scale score 3-6) outcomes at 90 days. These receiver operating characteristic curves were compared with those of previously reported predictors of favorable outcomes, such as the ΔNIHSS score (baseline NIHSS score—NIHSS score at 24 h), percent delta (ΔNIHSS score × 100/baseline NIHSS score), and early neurological improvement indices.

RESULTS: A total of 177 patients (median age, 72 years; female, 65 [37%]) were enrolled, and 109 (61.9%) had favorable outcomes. The respective sensitivity, specificity, and area under the curve values for an NIHSS of 10 were 92.6%, 80.7%, and .906; a ΔNIHSS score of 7 were 70.6%, 76.1%, and .797; and percent delta of 48.3% were 85.3%, 80.7%, and .890.

CONCLUSION: NIHSS score <10 at 24 hours after stroke onset is a strong predictor of favorable outcomes at 90 days in patients treated with MT.

KEY WORDS: Acute ischemic stroke, Mechanical thrombectomy, NIHSS, Outcome

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The efficacy of mechanical thrombectomy (MT) in patients with acute ischemic stroke with large vessel occlusion (LVO) has been reported by a meta-analysis of 5 randomized clinical trials.[1-5] The treatment approach for acute stroke with LVO has shifted from thrombolysis using recombinant tissue-type plasminogen activator (rt-PA) to MT.[6] Early prediction of clinical outcomes after thrombolysis or MT is important. Furthermore, early neurological improvement (ENI) is associated with favorable outcomes 90 days after stroke onset.[7-17] Indices of ENI after MT also reportedly suggest favorable outcomes.[18-20] However, almost all ENI indices as neurological improvement in the acute phase of stroke, but not patient outcome, and ENI indexes are associated with favorable outcomes in patients treated with rt-PA but not MT.

Recently, a few predictors for patient outcomes after MT had been reported.[18,21] Diffusion-weighted imaging is a known predictor,[22] but we use the National Institutes of Health Stroke Scale (NIHSS) score as a simple and convenient method without the use of special devices. We investigated whether the NIHSS score 24 hours after onset could accurately predict favorable outcomes at 90 days in patients with acute

ABBREVIATIONS: ASPECTS, Alberta Stroke Program Early CT Score; **BEST,** Blood Pressure After Endovascular Therapy for Ischemic Stroke; **ENI,** early neurological improvement; **LVO,** large vessel occlusion; **MRA,** MR angiography; **MT,** mechanical thrombectomy; **NIHSS,** National Institutes of Health Stroke Scale; **NPV,** negative predictive value; **PPV,** positive predictive value; **rt-PA,** recombinant tissue-type plasminogen activator; **SKIP,** Direct Mechanical Thrombectomy in Acute LVO Stroke; **TOAST,** Trial of ORG 10172 in Acute Stroke Treatment.

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stroke treated with MT compared with previously reported predictors.

METHODS

Patient imaging and clinical data were retrospectively selected from the Direct Mechanical Thrombectomy in Acute LVO Stroke (SKIP) study. The original trial was approved, and informed consent was provided by all the enrolled patients or their relatives. The SKIP study was an investigator-initiated, multicenter, randomized, open-label, noninferiority clinical trial of acute ischemic stroke due to LVO, conducted at 23 hospital networks in Japan from January 1, 2017, to July 31, 2019.[23] All patients in the SKIP study had LVO without large ischemic core lesions. Detailed inclusion and exclusion criteria have been reported previously.[24] Eligible patients were aged 18 to 85 years with acute ischemic stroke due to internal carotid artery occlusion or M1 occlusion confirmed on computed tomographic angiography (CTA) or MR angiography (MRA). A baseline Alberta Stroke Program Early CT Score (ASPECTS) of 6 to10, diffusion-weighted imaging–ASPECTS of 5 to 10, and NIHSS of 6 or greater, were functionally independent (the modified Rankin Scale [mRS] score of 0–2) before stroke. The criteria of the Japanese guidelines for treatment with the lower dose of 0.6 mg/kg of alteplase as intravenous thrombolysis within 4.5 hours of onset of symptoms was used for alteplase administration. Additional exclusion criteria for this study were as follows: (1) nonperformance of MT and (2) undocumented NIHSS score 24 hours after treatment.

Collected Variables

The following clinical information was obtained from the SKIP data set: sex; age; body weight; height; blood pressure on arrival; heart rate on arrival; neurological deficit (NIHSS score on admission and 24 hours after onset); modified Rankin Scale (mRS) score before stroke and 90 days after stroke; vascular risk factors (hypertension, dyslipidemia, and diabetes mellitus); atrial fibrillation; smoking; past stroke; past cardiovascular disease; medication on admission (antiplatelet or anticoagulant agents); ASPECTS (on computed tomography and diffusion-weighted magnetic resonance imaging); arterial occlusion site on anterior circulation; stroke etiology; time intervals of onset-to-door, onset-to-random, random-to-puncture, and puncture-to-reperfusion; reperfusion status; number of MT procedures represented as pass; and symptomatic intracranial hemorrhage after MT.

Clinical Definitions and Outcome Measures

The functional outcome was estimated using the mRS, and favorable outcomes at 90 days after stroke onset were defined as an mRS score of 0 to 2. Reperfusion status was estimated after MT using the expanded Treatment in Cerebral Ischemia scale, and a grade ≥2b was defined as successful reperfusion.[25] Stroke etiology was estimated using the Trial of ORG 10172 in Acute Stroke Treatment (TOAST) criteria as follows: (1) large-artery atherosclerosis, (2) cardioembolism, and (3) other or undetermined etiology of stroke.[26] Symptomatic intracranial hemorrhage after MT was estimated using the Safe Implementation of Thrombolysis in Stroke-Monitoring Study protocol as local or remote parenchymal hemorrhage type 2, combined with a neurological deterioration of ≥4 points on the NIHSS score from baseline.[26]

Statistical Analyses

First, patients were assigned into 2 groups according to clinical outcomes. Clinical background characteristics were compared between patients with favorable (mRS score 0-2) and poor outcomes (mRS score 3-6).

Second, the optimal cut-off NIHSS score 24 hours after onset was calculated using receiver operating characteristic (ROC) curves to predict favorable and poor outcomes 90 days after onset. We compared this cut-off NIHSS score with other previously reported predictors, such as the ΔNIHSS score (baseline NIHSS score—NIHSS score at 24 hours) and the percent delta (ΔNIHSS score × 100/baseline NIHSS score). The optimal cut-off NIHSS score at the ΔNIHSS score and percent delta were obtained by constructing ROC curves.

Third, the cut-off NIHSS score was compared with the previously reported ENIs. The definitions of ENI 24 hours after treatment in previous reports[7-12] were as follows: (1) NIHSS score <4 on follow-up or improvement ≥10 points from the baseline NIHSS score; (2) NIHSS score of 0 or 1 on follow-up or improvement ≥8 points from the baseline NIHSS score; (3) improvement ≥4 points from the baseline NIHSS score; (4) improvement of 20% from the baseline NIHSS score; (5) improvement by 40% from the baseline NIHSS score; and (6) NIHSS score 0 to 1.

All statistical analyses were performed using the SPSS software, version 27 (SPSS Japan, Inc.). The results were considered statistically significant at $P < .05$. Univariate analyses were performed using the χ^2 and Mann-Whitney U tests, as appropriate. Data are presented as median values and IQR, and categorical variables are presented as frequencies and percentages.

RESULTS

Of 204 patients, 5 with no MT treatment and 22 without documented NIHSS scores 24 hours after treatment were excluded. Ultimately, 177 patients were included in this study. The median age was 72 years, and 65 patients (37%) were women. The baseline patient characteristics shown in Table 1 are as follows: Hypertension was observed in 107 patients (60%), hyperlipidemia in 59 (33%), and atrial fibrillation in 108 (61%). Intravenous rt-PA was administered to 91 patients (51%). Most strokes were due to either large-artery atherosclerosis (18%) or cardioembolism (71%). The median baseline NIHSS score was 18 (IQR, 12-23), and the median ASPECTS score was 8 (IQR, 6-9).

Favorable outcomes 90 days after onset were observed in 109 (62%) of the 177 patients. The clinical characteristics of the 2 groups are shown in Table 2. Prestroke mRS score 2 ($P = .02$), ASPECTS ($P = .014$), large-artery atherosclerosis ($P = .013$), cardioembolism ($P = .017$), expanded Treatment in Cerebral Ischemia grade ≥2b ($P = .007$), ΔNIHSS scores ($P < .001$), and percent delta scores ($P < .001$), age ($P = .002$), baseline NIHSS score ($P < .001$), onset-to-door time ($P = .002$), number of pass ($P = .004$), NIHSS score 24 hours after MT ($P < .001$), and symptomatic intracranial hemorrhage rate after MT ($P = .005$) were found between the two groups. No significant differences in sex, medical history, antithrombotic medication on admission, occlusion site, use of rt-PA, or stent retrieval first pass were found between the 2 groups. Figure 1 shows the scatter diagram of the relationship between the baseline NIHSS score and NIHSS score 24 hours after MT.

TABLE 1. Clinical Characteristics With mRS 0-2 and mRS 3-6

Variables	mRS 0-2 n = 109	mRS 3-6 n = 68	*P* value
Female sex, n (%)	39 (35.8)	26 (38.2)	.742
Age, median (IQR), years	73 (67-78)	76 (71-82)	.002
Body weight, median (IQR), kg	59 (52-66)	60 (52-72)	.575
Height, median (IQR), cm	161 (157-170)	163 (157-170)	.675
Systolic blood pressure on arrival, median (IQR), mmHg	154 (136-169)	151 (130-172)	.959
Diastolic blood pressure on arrival, median (IQR), mmHg	85 (77-94)	83 (77-103)	.609
Heart rate, median (IQR), min	80 (67-96)	89 (72-98)	.057
mRS score before stroke, n (%)			
0	96 (88.9)	53 (77.9)	.05
1	10 (9.3)	6 (8.8)	.922
2	2 (1.9)	9 (13.2)	.02
Medical history, n (%)			
Hypertension	68 (62.4)	39 (57.4)	.505
Hyperlipidemia	35 (31.5)	24 (36.8)	.47
Diabetes mellitus	12 (11.0)	13 (19.1)	.132
Atrial fibrillation	69 (63.3)	49 (57.4)	.43
Smoking	46 (42.2)	36 (52.9)	.163
Past stroke	12 (11.0)	9 (13.2)	.656
Past cardiovascular disease	8 (7.3)	4 (5.9)	.708
Medication on admission, n (%)			
Antiplatelet agent	18 (16.5)	12 (17.6)	.845
Anticoagulant agent	19 (16.5)	12 (17.6)	.845
Baseline NIHSS score, median (IQR)	16 (11-21)	21 (17-25)	<.001
ASPECTS, median (IQR)	8 (6-9)	7 (5-9)	.014
Occlusion site, n (%)			
Internal carotid artery	35 (32.1)	29 (42.6)	.156
Middle cerebral artery M1 proximal	23 (21.1)	12 (17.6)	.575
Middle cerebral artery M1 distal	51 (46.8)	27 (39.7)	.356
TOAST classification, n (%)			
Large-artery atherosclerosis	13 (11.9)	18 (26.5)	.013
Cardioembolism	84 (77.1)	41 (60.3)	.017
Other determined/undetermined etiology	12 (11.0)	9 (13.2)	.656
Onset-to-door time, median (IQR), min	71 (44-121)	118 (58-150)	.002
Door-to-random time, median (IQR), min	33 (25-48)	31 (20-45)	.409
Random-to-puncture time, median (IQR), min	18 (12-25)	17 (11-23)	.807
Puncture-to-reperfusion time, median (IQR), min	30 (21-42)	39 (22-61)	.067
rt-PA, n (%)	55 (50.5)	36 (52.9)	.748
Stent retriever first pass, n (%)	64 (58.7)	37 (54.4)	.574
eTICI ≥ 2b, n (%)	106 (97.2)	59 (86.8)	.007
Pass times, median (IQR)	1 (1-2)	2 (1-2)	.004
NIHSS score 24 h after MT, median (IQR)	4 (2-8)	17 (11-21)	<.001
ΔNIHSS score, median (IQR)	10 (7-14)	4 (1-8)	<.001
Percent delta, median (IQR), %	67 (50-88)	16 (−3 to 42)	<.001
Symptomatic intracranial hemorrhage after MT, n (%)	2 (1.1)	8 (11.8)	.005

ASPECTS, Alberta Stroke Program Early CT Score; mRS, modified Rankin Scale; MT, mechanical thrombectomy; NIHSS, National Institutes of Health Stroke Scale; rt-PA, recombinant tissue-type plasminogen activator; eTICI, expanded Treatment in Cerebral Ischemia scale.

We also tested multivariable analysis with age, sex (male), ASPECTS, TOAST classification (large-artery atherosclerosis), onset-to-door time, expanded Treatment in Cerebral Ischemia grade ≥2b, symptomatic intracranial hemorrhage, and various NIHSS (**Supplemental Table, Model 1-4**, http://links.lww.com/NEU/D351). NIHSS score of <10 at 24 hours (odds ratio [OR] 45.101, 95% CI 14.947-136.093, $P < .001$) associated with mRS score 0 to 2 at 90 days (**Supplemental Table, Model 1**, http://links.lww.com/NEU/D351). NIHSS score at 24 hours (OR 0.759, 95% CI 0.692-0.831, $P < .001$) associated with mRS score 0 to 2 at 90 days (**Supplemental Table, Model 2**, http://links.lww.com/NEU/D351). ΔNIHSS (OR 0.812, 95% CI 0.748-0.882, $P < .001$) and age (OR

TABLE 2. Comparison of Early Neurological Improvement Definitions, NIHSS Score < 10, ΔNIHSS Score ≥ 7, and Percent Delta ≥48.3% in this Study

Definitions	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	AUC (%)	95% CI
NIHSS < 4 on follow-up or improvement ≥10 from baseline NIHSS score	70.6	77.9	85.9	62.4	0.743	0.667-0.819
NIHSS 0 or 1 on follow-up or improvement ≥8 from baseline NIHSS score	73.4	73.5	83.7	63.3	0.735	0.657-0.812
Improvement ≥4 points from baseline NIHSS score	90.8	47.1	73.3	76.2	0.689	0.605-0.774
Improvement by 20% from baseline NIHSS score	91.7	57.4	76.7	81.3	0.745	0.665-0.826
Improvement by 40% from baseline NIHSS score	82.6	73.5	71.3	72.5	0.780	0.707-0.854
NIHSS score 0 to 1	22.0	100.0	100.0	44.4	0.610	0.528-0.692
NIHSS score < 10	92.6	80.7	94.6	75.0	0.906	0.862-0.949
ΔNIHSS score ≥ 7	70.6	76.1	80.6	64.9	0.797	0.730-0.865
Percent delta ≥ 48.3%	85.3	80.7	81.9	74.4	0.890	0.842-0.937

AUC, area under curve; NIHSS, National Institutes of Health Stroke Scale; NPV, negative predictive value; PPV, positive predictive value.

0.937, 95% CI 0.896-0.980, $P = .004$) associated with mRS score 0 to 2 at 90 days (**Supplemental Table, Model 3**, http://links.lww.com/NEU/D351). Percent delta (OR 0.952, 95% CI 0.936-0.967, $P < .001$), age (OR 0.940, 95% CI 0.890-0.993, $P = .026$), and symptomatic intracranial hemorrhage (OR 13.239, 95% CI 1.136-154.247, $P = .036$) associated with mRS score 0 to 2 at 90 days (**Supplemental Table, Model 4**, http://links.lww.com/NEU/D351).

The cut-off NIHSS score at 24 hours after MT was 10, with a sensitivity of 80.7%, specificity of 92.6%, positive predictive value (PPV) of 94.6%, negative predictive value (NPV) of 75.0%, and area under the curve (AUC) of .906 (**Supplemental Figure A**, http://links.lww.com/NEU/D352). The cut-off point of the ΔNIHSS score was 7 with a sensitivity, 70.6%; specificity, 76.1%; PPV, 81.1%; NPV, 58.6%; and AUC, .797

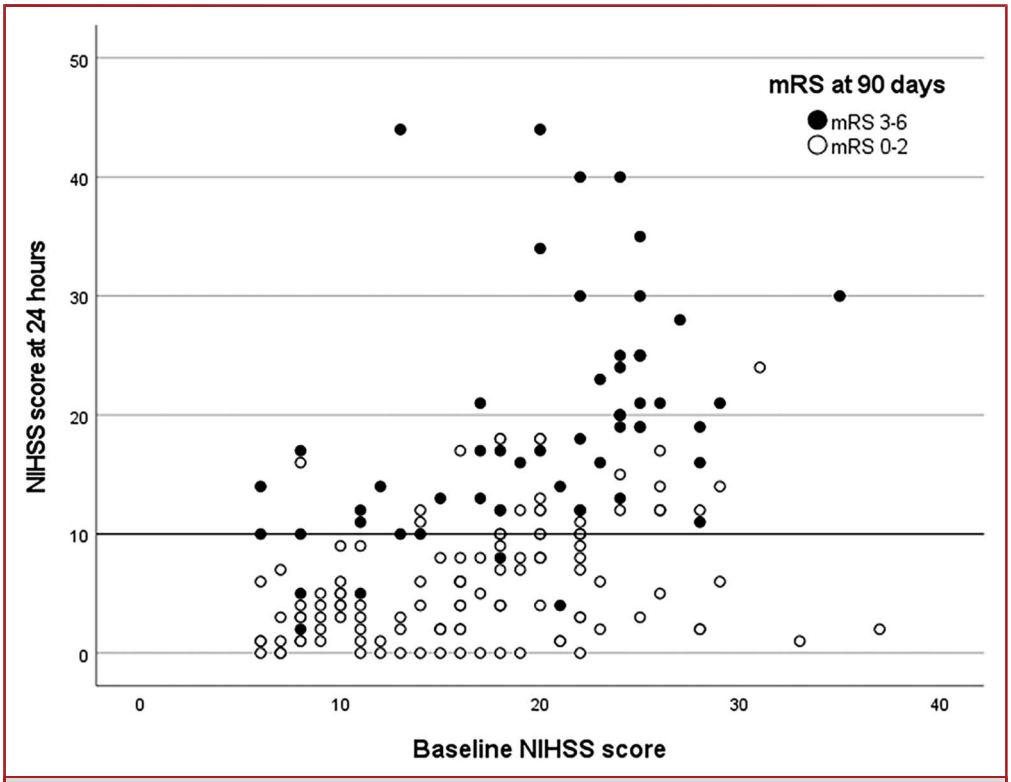

FIGURE 1. *Scatter diagram showing the relationship between the NIHSS score at 24 h and mRS score at 90 days. Of the patients with NIHSS score <10 at 24 h after mechanical thrombectomy, 88 (94.6%) presented with an mRS score of 0 to 2 at 90 days. mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale.*

(**Supplemental Figure B**, http://links.lww.com/NEU/D352). The cut-off point of the percent delta was 48.3%, with a sensitivity of 85.3%, specificity of 82.6%, PPV of 81.9%, NPV of 74.4%, and AUC of .890 (**Supplemental Figure C**, http://links.lww.com/NEU/D352). Figure 2 categorizes the patients according to NIHSS score <10 or ≥10 at 24 hours after onset and their outcomes at 90 days after onset.

Using the ROC curve, the AUCs of ENI indices as predictors of favorable outcomes were as follows: An NIHSS score <4 on follow-up or an improvement ≥10 points from the baseline NIHSS score was .74; an NIHSS score of 0 or 1 on follow-up or an improvement ≥8 points from the baseline NIHSS score was .735; an improvement ≥4 points from the baseline NIHSS score was .689; an improvement of 20% from the baseline NIHSS score was .745; an improvement of 40% from the baseline NIHSS score was .780; and an NIHSS score of 0 to 1 was .610.

Therefore, an NIHSS score of <10 at 24 hours was a stronger predictor of favorable outcomes than the ΔNIHSS score, percent delta, and ENI indices (Table 2).

DISCUSSION

We investigated whether the NIHSS score at 24 hours after stroke onset could accurately predict favorable outcomes at 90 days and found that an NIHSS score <10 at 24 hours after onset was the best predictor of favorable outcomes in patients with LVO treated using MT.

Using the Blood Pressure After Endovascular Therapy for Ischemic Stroke (BEST) cohort study, Mistry et al[27] also reported that a cut-off NIHSS score of seven 24 hours after onset is a good predictor of favorable outcomes with a sensitivity of 80.1% and specificity of 80.4%.[28] In our study, an NIHSS score <10 at 24 hours after onset had a sensitivity of 92.6%, specificity of 80.7%, and AUC of .906 to predict favorable outcomes. In our data, when an NIHSS score ≤ 7 was used to predict favorable outcomes, sensitivity, specificity, and AUC were 69.7%, 94.1%, and .819, respectively. Therefore, from our data, an NIHSS score <10 was a better predictor than an NIHSS score ≤ 7. This difference may be due to variations in the backgrounds of patients included in the original studies. The SKIP study included patients with internal carotid artery or M1 occlusion and a median NIHSS score of 18 at admission,[24] whereas the BEST study included patients with internal carotid artery or M1 or M2 occlusion and a median NIHSS score of 16 at admission.[27] This study in a group of patients for whom MT has been shown to be an effective treatment may be more useful.

In our study, 94.6% of patients with an NIHSS score <10 at 24 hours after onset had favorable outcomes, and only 6.4% had unfavorable outcomes. The ΔNIHSS score and percent delta are

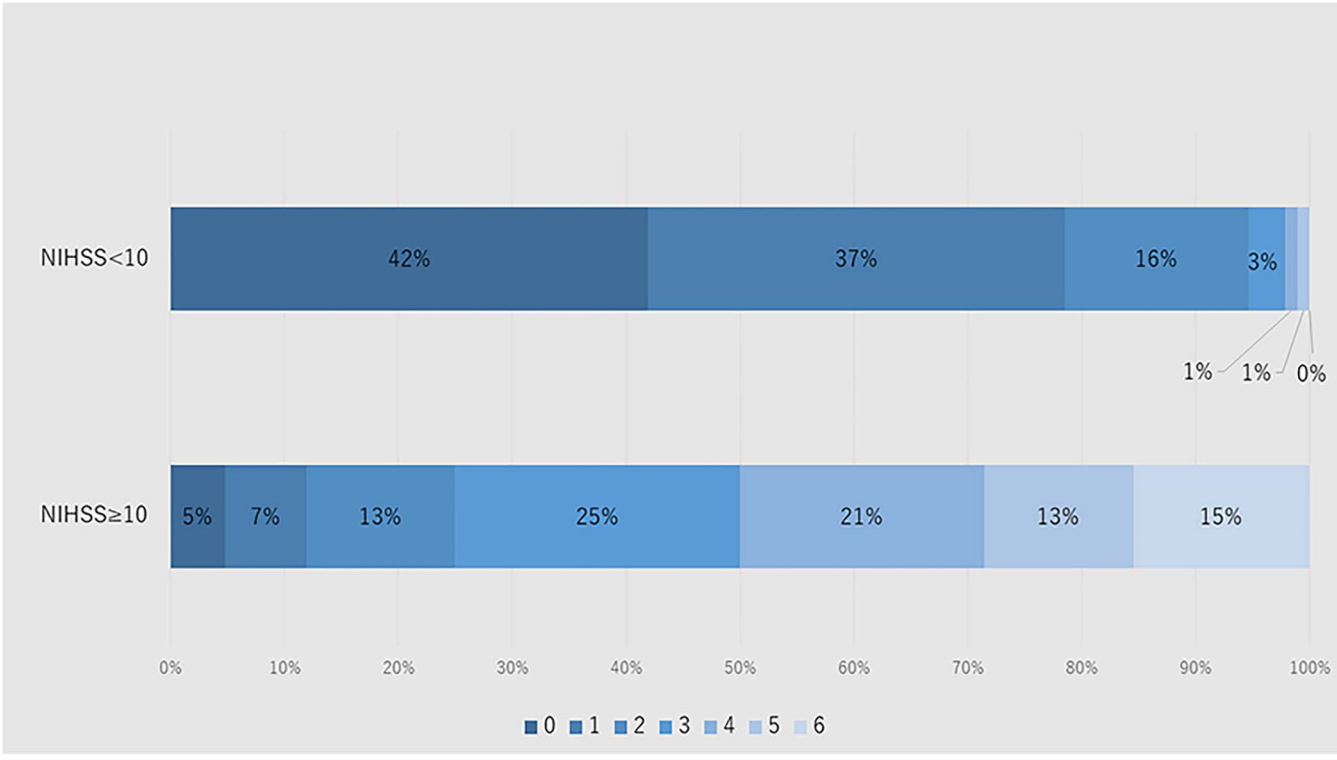

FIGURE 2. *Functional outcomes at 90 days according to the mRS score. There were significant differences between patients with the NIHSS scores <10 and NIHSS scores ≥10 (P < .001) regarding favorable outcomes at 90 days, defined as an mRS score of 0 to 2. mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale.*

good predictors of neurological improvement, but not clinical outcomes. For example, the ΔNIHSS score of a patient with improvement from a baseline NIHSS score of 10 to a follow-up NIHSS score of 2 is 8, but the ΔNIHSS score of a patient with improvement from a baseline NIHSS score of 30 to a follow-up NIHSS score of 22 is also 8. Despite both patients having a ΔNIHSS score of 8 and improvements in neurological symptoms, the first patient had a favorable outcome, whereas the latter had a poor outcome. The percent delta is calculated to correct the ΔNIHSS score using the baseline NIHSS score. Therefore, the percent delta and ΔNIHSS scores represent improvements in neurological symptoms but not a prediction of clinical outcomes.

ENIs are known as early outcome predictors in acute cerebral infarction and are linked to favorable outcomes at 90 days.[7-20] ENI indices are measures of neurological improvement during the acute phase of stroke; however, they cannot directly predict patient outcomes. In this study, ENI indices were not better predictors of favorable outcomes than NIHSS scores <10 at 24 hours after onset.

Clinical factors of ENI for rt-PA and MT therapy include a high ASPECTS,[12,15-17] short time between onset and treatment,[9,12,14,16] high rate of successful recanalization,[7,8,10,11,13,15,17] effective first-pass recanalization,[28] hemorrhagic transformation,[29] admission high blood pressure,[30] and low prestroke mRS score.[31] In this study, a high ASPECTS, short onset-to-door time, high rate of effective recanalization, few pass times, low prestroke mRS scores, and few symptomatic intracranial hemorrhages after MT were also significantly more common in the favorable outcome group. However, such factors are associated with favorable outcomes but are not directly predictors of outcome. Other reports use age and NIHSS as predictors of outcome[32] or factors that predict poor outcome in spite of good NIHSS,[33] but an NIHSS score <10 at 24 hours after MT is a very simple and easily measured index and useful predictor of favorable outcomes.

Limitations

This study has some limitations. First, the sample size was small. Second, our study included only patients treated for anterior circulation stroke due to LVO. Third, the SKIP trial is an RCT study, and it is possible that the enrolled patients should have more favorable outcomes than we expected because of fewer complications. Therefore, NIHSS<10 may be a little low point in the real world. Fourth, 2 patients significantly improved in 24 hours but have poor mRS in this study. The reason was not clear, but we suspect that 2 cases might have diseases with worsened activities of daily living such as stroke recurrence, heart failure, or fractures several days after MT. Fifth, this study was conducted based on the NIHSS score at 24 hours, but not at 6 hours and 12 hours. This was because ENI indices were applied 24 hours after onset. NIHSS scores 6 hours and 12 hours after onset may be more appropriate predictors of favorable outcomes than at 24 hours; this warrants further investigation. Sixth, mean platelet volume/platelet count ratio in patients with large-artery atherosclerosis also is reported to be associated with patient outcome,[34] but unfortunately the SKIP study did not have such data. Seventh, collaterals were also reported to be related to be associated with patient outcome[35,36] but were not fully examined in this study.

CONCLUSION

After MT for acute stroke with LVO, an NIHSS score of <10 points at 24 hours after stroke onset is a strong predictor of favorable outcomes at 90 days.

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Supplemental Digital Content 1. Supplemental Table. Multiple logistic regression analyses of factors associated with 90-day favorable outcomes. There were 4 models for multivariable analysis with age, ASPECTS, onset-to-door time, TICI2b, symptomatic intracranial hemorrhage, and various NIHSS. Model 1 was studied using an NIHSS score of <10 at 24 h, Model 2 using the baseline NIHSS score, Model 3 using the NIHSS score at 24 h, and Model 4 using delta NIHSS.
Supplemental Digital Content 2. Supplemental Figure. Receiver operating characteristics of National Institutes of Health Stroke Scale (NIHSS)–based outcome measures at predicting 90-day modified Rankin Scale (mRS) 0 to 2. A, NIHSS score at 24 hours, B, ΔNIHSS score, C, percent delta. The sensitivity (*y* axis) and 1-specificity (*x* axis) and the area under the curve for NIHSS score at 24 hours, ΔNIHSS score, and percent delta at differentiating 90-day mRS score 0 to 2 vs 3 to 6 is shown.