

## Original Article

## Prehospital triage for endovascular clot removal in acute stroke patients

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**Aim:** To establish prehospital triage in accordance with the new guidelines for endovascular therapy, we retrospectively analyzed the monitoring data of the city-wide transportation system using the Maria Prehospital Stroke Scale (MPSS), a novel prehospital stroke scale for emergency medical technicians (EMTs) to predict the likelihood of thrombolytic therapy after transportation.

**Methods:** Kawasaki City, Japan, has six comprehensive stroke centers (CSCs) and six primary stroke centers (PSCs). In CSCs, endovascular therapy can be carried out 24 h a day, 7 days a week, but not in PSCs. There is no “drip and ship” protocol for further endovascular therapy from PSCs to CSCs. We determined the predictive value of MPSS scoring by the EMTs for the performance of endovascular therapy after transportation.

**Results:** There were 2031 patients (mean age, 71.1 ± 13.3 years) registered from April 2012 to March 2015. Multivariate logistic regression analysis indicated that the MPSS score and type of stroke center were independent predictors for performance of endovascular therapy. In particular, the odds ratio (OR) for endovascular therapy was significant for MPSS score 3 (OR, 2.914; 95% confidence interval (CI), 1.152–7.372; *P* = 0.024), MPSS score 4 (OR, 5.474; 95%CI, 2.300–13.029; *P* = 0.000), and MPSS score 5 (OR, 11.459; 95%CI, 4.334–30.296; *P* = 0.000) when MPSS score 1 was set as a reference. The diagnostic accuracy of the MPSS score evaluated by EMTs was 0.689 (95%CI, 0.627–0.751).

**Conclusions:** Prehospital triage using MPSS scores evaluated by EMTs can predict the likelihood of performance of endovascular therapy after transportation, and may become a tool offering a flexible solution for designing a new transportation protocol.

**Key words:** Endovascular therapy, prehospital, stroke, stroke-bypass transportation, thrombolysis

## INTRODUCTION

EVIDENCE TO DATE indicates that certain endovascular procedures provide clinical benefit in selected patients with acute ischemic stroke.<sup>1–5</sup> To facilitate rapid access to qualified neurointerventionalists, remodeling of the

existing regional acute stroke care system is an urgent task. Recently revised guidelines<sup>6,7</sup> recommend that endovascular therapy should be initiated (groin puncture) within 6 h of symptom onset. Stroke-bypass transportation to the stroke center by paramedics is important to maximize the efficacy of thrombolytic therapy using i.v. tissue plasminogen activator (iv-tPA) and endovascular therapy. The Maria Prehospital Stroke Scale (MPSS) is a novel prehospital stroke scale for emergency medical technicians (EMTs) to predict the likelihood of the performance of thrombolytic therapy after transportation.<sup>8</sup> In Kawasaki City, Japan (population of 1,431,094 people over an area of 142.7 km<sup>2</sup>), a citywide transportation protocol for stroke was launched in January

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2009 to improve access to stroke thrombolysis using the MPSS, and quality assurance monitoring has been carried out every 6 months since April 2009.<sup>9</sup> To investigate pre-hospital triage in accordance with the new guidelines for endovascular therapy, we retrospectively analyzed the monitoring data.

## MATERIALS AND METHODS

**I**N KAWASAKI CITY, there are 12 hospitals that accept stroke bypass transfers for iv-tPA therapy. In six of them, endovascular therapy is not routinely carried out. In the other six hospitals, endovascular therapy is performed in 24 h/7 day fashion. Although there is no formal definition or categorization of primary and comprehensive stroke centers in Japan, we analyzed the data by categorizing the former six hospitals as primary stroke centers (PSCs) and the latter hospitals as comprehensive stroke centers (CSCs).

## Maria Prehospital Stroke Scale and transportation protocol

The clinimetric characteristics of the MPSS have been described in detail elsewhere.<sup>7,8</sup> Briefly, the MPSS was developed by modifying the Cincinnati Prehospital Stroke Scale (CPSS). In using the CPSS, facial droop, arm drift, and speech disturbance are tested by EMTs. Facial droop is graded as normal (0) or abnormal (1), and the other two items are graded in three levels, as normal (0), not severe (1), or severe (2). Thus, the total MPSS score ranges from 0 to 5 (Table 1), but basically MPSS  $\geq 1$  is analogous to CPSS  $\geq 1$  for the diagnosis of stroke. A significant correlation between the MPSS score by EMTs and National Institutes of Health Stroke Scale (NIHSS) scores by physicians simultaneously evaluating the same patient in the emergency room was confirmed (Spearman's  $\rho = 0.89$ ,  $P < 0.001$ ). The MPSS scored by EMTs was also significantly correlated with NIHSS score in the emergency room (Spearman's

**Table 1.** Characteristics and treatment of patients with acute ischemic stroke in Kawasaki City, Japan, April 2012 to March 2015

	Primary stroke center	Comprehensive stroke center	P-value
Total number of transferred patients, <i>n</i>	565	1466	
Male sex, <i>n</i> (%)	373 (66.0%)	957 (63.5%)	0.398
Age, years, mean $\pm$ SD	71.6 $\pm$ 13.6	71.0 $\pm$ 13.5	0.377
MPSS, mean $\pm$ SD (median, min–max)	2.5 $\pm$ 1.5 (3, 0–5)	2.6 $\pm$ 1.4 (3, 0–5)	0.407
Score 0, <i>n</i> (%)	65 (11.5)	124 (8.5)	
Score 1, <i>n</i> (%)	108 (19.1)	263 (17.9)	
Score 2, <i>n</i> (%)	100 (17.7)	281 (19.2)	
Score 3, <i>n</i> (%)	91 (16.1)	320 (21.8)	
Score 4, <i>n</i> (%)	163 (28.8)	396 (27.0)	
Score 5, <i>n</i> (%)	38 (6.7)	82 (5.6)	
Detection-to-door time, mean $\pm$ SD (min–max) min	34.4 $\pm$ 11.6	34.3 $\pm$ 10.6	0.835
Onset-to-door time, mean $\pm$ SD (min–max) min	340.7 $\pm$ 805.2	280.1 $\pm$ 797.8	0.154
Door-to-needle time, mean $\pm$ SD (min–max) min	89.1 $\pm$ 35.0	81.0 $\pm$ 27.9	0.874
Diagnosis			
Cerebrovascular diseases, <i>n</i> (%)	433 (76.6)	1189 (81.1)	0.253
Brain infarction, <i>n</i> (%)	295 (55.0)	778 (53.1)	0.344
Treatment for brain infarction			
iv-tPA only, <i>n</i> (%)	41 (13.9)	96 (12.2)	0.000
iv-tPA + endovascular therapy, <i>n</i> (%)	5 (1.7)	48 (6.1)	
Endovascular therapy only, <i>n</i> (%)	4 (1.4)	56 (7.1)	
NIH Stroke Scale score			
Before treatment	10.05 $\pm$ 8.63	11.01 $\pm$ 8.15	0.215
24 h after therapy	8.11 $\pm$ 8.80	8.87 $\pm$ 7.33	0.479
One month after treatment	6.05 $\pm$ 7.81	5.62 $\pm$ 7.68	0.651
Premorbid Rankin Scale score	0.57 $\pm$ 1.2	0.56 $\pm$ 1.2	0.880
Modified Rankin Scale score 1 month after onset	2.45 $\pm$ 1.96	2.54 $\pm$ 1.81	0.590

iv-tPA, i.v. therapy using tissue plasminogen activator; MPSS, Maria Prehospital Stroke Scale; NIH, National Institutes of Health; SD, standard deviation.

$\rho = 0.67$ ,  $P < 0.001$ ). The rate of performance of thrombolytic therapy increases when the MPSS score increases from 0 to 5: 0%, 4.1%, 8.8%, 13.0%, 20.3%, and 31.5%, respectively.<sup>7</sup> The accuracy for the diagnosis of stroke by the EMTs and accuracy for the prediction of thrombolysis using iv-tPA after transportation were 0.737 (95% confidence interval [CI], 0.688–0.786) and 0.689 (95% CI, 0.645–0.732), respectively.<sup>7</sup> In the MPSS-based transportation protocol, EMTs are required to prenotify the receiving hospital of the MPSS score. The patients with MPSS score  $\geq 1$  and within the therapeutic time window should be transferred to the nearest hospital authorized for iv-tPA. Emergency medical technicians recorded the time that symptom onset was discovered and the stroke onset times were recorded by the attending physician as the time the patient was last known to be well. This is the all-case surveillance study for the quality assurance monitoring and all patients transferred by the MPSS transportation protocol were recorded without any exclusion criteria. In this study, the patients with MPSS score = 0 may be transferred to the hospitals when the EMTs suspected transient ischemic attack or minor stroke.

All the MPSS-based transportation data were recorded by the Kawasaki City Fire Department in an Excel file (Microsoft Corporation, Tokyo, Japan) and the clinical data of the patients who were transported to each hospital were added to this file as linkable anonymizing data while adhering to the fire laws in Japan. After the unlinkable anonymization of this file, statistical analysis for the quality assurance monitoring was carried out every 6 months by the Department of Neurology, St. Marianna University (Kawasaki, Japan), a secretariat of the Kawasaki Stroke Network. Informed consent was waived because of the anonymous nature of the data. Because of these regulations, any intervention study or follow-up study beyond the acute stage was not permitted. This study was approved by the St. Marianna University Bioethics Committee (#2509).

Prehospital clinical indicators such as onset-to-dispatch, onset-to-door, and onset-to-needle time, and hospital clinical indicators such as door-to-needle time, frequency of thrombolytic use, and outcome of thrombolytic therapy were included in this dataset. In Japan, commercial use of the Merci Retriever<sup>®</sup> (Concentric Medical, Mountain View, California, USA) started in April 2010 in Japan. Then, approval was granted for the Penumbra System<sup>®</sup> (Penumbra Alameda, California, USA) in 2011, the Solitaire<sup>™</sup> Flow Restoration device (Covidien/ev3, Dublin, Ireland) in 2014, and the Trevo Pro Retriever (Stryker Neurovascular, Fremont, CA) in 2014. Performance of endovascular therapy has been recorded in the Kawasaki Stroke Network registry since April 2012. Therefore, endovascular therapy was carried out mainly by the Merci Retriever or the Penumbra

System. Endovascular therapy was undertaken only in the patients transferred to each hospital at the discretion of treated physicians, because all the patients were admitted before publication of the new guidelines for endovascular therapy.<sup>10</sup> However, the Merci Retriever and the Penumbra System were approved for use in the revascularization of patients with acute ischemic stroke secondary to intracranial large vessel occlusive disease within 8 h of symptom onset. There was no “drip and ship” protocol for further endovascular therapy from PSCs to CSCs. We retrospectively analyzed the dataset from 2012 to 2015.

All patients underwent computed tomography or magnetic resonance imaging. The NIHSS score<sup>11</sup> was recorded at hospital arrival, 24 h after injection of tPA and/or endovascular therapy, and 1 month after onset or at discharge in patients with ischemic stroke who received iv-tPA or endovascular therapy. The Rankin Scale score before onset and the modified Rankin Scale (mRS) score<sup>12</sup> at 1 month after onset or at discharge were recorded. The mRS score at 3 months after onset was not obtained because the present study was carried out as quality assurance monitoring while adhering to fire department regulations in Japan. Using the database mentioned above, the Kawasaki Stroke Network hospitals and the fire department undertake continued quality assurance monitoring every 6 months.

## Statistical analyses

The unpaired Student's *t*-test was used to compare continuous variables, and Pearson's  $\chi^2$ -test was used for nominal parameters. The Mann–Whitney *U*-test was used for data that were not normally distributed. Multivariate logistic regression analysis was carried out to determine independently associated factors evaluated in the prehospital setting. Diagnostic accuracies of MPSS scoring by EMTs and NIHSS scoring evaluated by attending physicians were tested by receiver–operating characteristic curve analysis. All statistical analyses were carried out using IBM SPSS Statistics for Windows version 22 software (Chicago, IL, USA). All statistical tests were two-sided, and probability values  $<0.05$  were considered significant.

## RESULTS

### Patient characteristics

A TOTAL OF 2031 patients were registered from April 2012 to March 2015. Their characteristics are shown in Table 1. Their mean age was  $71.1 \pm 13.3$  years (minimum–maximum, 24–98 years), and 65.5% of them were men. Of these patients, 565 (27.8%) were transferred to

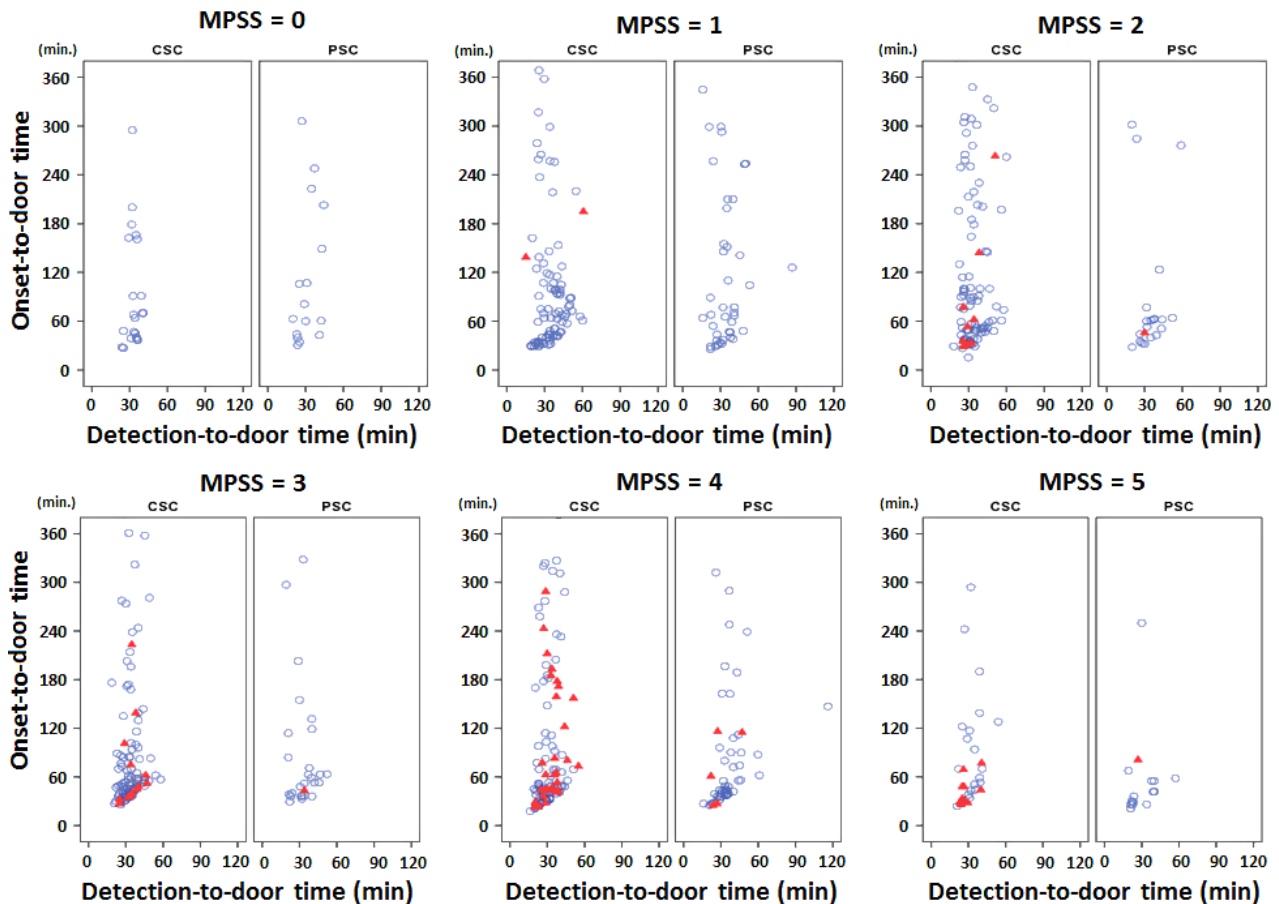
PSCs and the remainder (72.2%) were transferred to CSCs. Age, sex, MPSS score, detection-to-door time, and frequencies of cerebrovascular diseases or brain infarction diagnosed after transportation were similar between the patients treated in PSCs and CSCs. In patients with brain infarction, onset-to-door time and NIHSS score before, 24 h after, and 1 month after the treatment were similar. The premorbid Rankin Scale score and the mRS score were similar. However, the frequency of endovascular therapy in CSCs was significantly higher than that in PSCs ( $P = 0.000$ ).

The relationship between endovascular therapy and prehospital delay according to MPSS score and type of stroke center is shown in scattergrams in Figure 1. No endovascular therapy was undertaken in patients with MPSS score 0, and 104 of 113 patients with endovascular therapy (92.0%) received treatment in CSCs (red triangles). In patients with an MPSS score ranging from 2 to 5, endovascular therapy was also carried out in the PSCs, but patients with delayed

admission (onset-to-door time  $>120$  min) did not receive endovascular therapy in the PSCs. The performance rate of endovascular therapy according to MPSS score and type of hospital in patients with ischemic stroke and admission within 6 h (onset-to-door time  $<360$  min) are shown in Figure 2. The performance rate increased along with the MPSS score in CSCs from 4.6% for patients with MPSS score 1, to 33.3% in patients with MPSS score 5.

### Multivariate logistic regression analysis

In patients transferred to 12 hospitals with MPSS score  $\geq 1$ , univariate logistic regression analysis showed that MPSS score evaluated by EMTs, type of stroke center, and onset-to-door time were significantly associated with performance of endovascular therapy after admission. Multivariate analysis showed that MPSS score and type of stroke center were independent predictors for the performance of endovascular



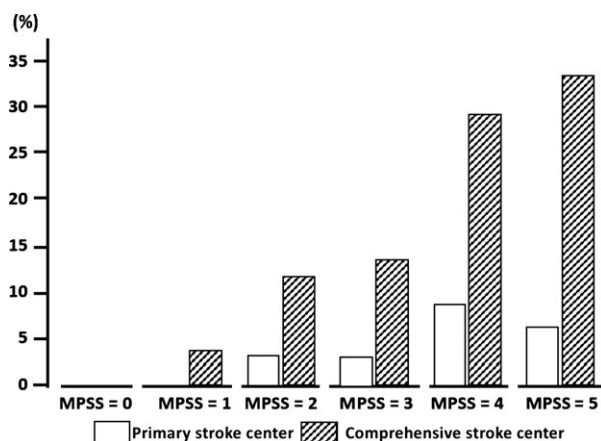
**Fig. 1.** Scattergrams showing the relationship between endovascular therapy and prehospital delay by Maria Prehospital Stroke Scale (MPSS) score and type of stroke center. Red triangles and open circles denote the patients with and without endovascular therapy, respectively. CSC, comprehensive stroke center; PSC, primary stroke center.

therapy (Table 2). In particular, the odds ratios (ORs) for endovascular therapy were significant for MPSS score 3 (OR, 2.914; 95% CI, 1.152–7.372;  $P = 0.024$ ), MPSS score 4 (OR, 5.474; 95% CI, 2.300–13.029;  $P = 0.000$ ), and MPSS score 5 (OR, 11.459; 95% CI, 4.334–30.296;  $P = 0.000$ ) when MPSS score 1 was set as a reference.

The diagnostic accuracy of the MPSS score evaluated by EMTs and the NIHSS score just before treatment as evaluated by attending physicians for predicting endovascular therapy was examined using receiver–operating characteristic analysis. The areas under the curve for MPSS score and NIHSS score were similar, 0.689 (95% CI, 0.627–0.751) and 0.678 (95% CI, 0.616–0.740), respectively (Fig. 3).

## DISCUSSION

**T**OOLS TO DETERMINE the presence of stroke in patients have thus far included the CPSS and the Los Angeles Prehospital Stroke Screen;<sup>13</sup> however, the MPSS is the only tool that can evaluate the likelihood of performing thrombolytic therapy after transportation.<sup>8</sup> The present study evaluated the clinimetric properties of the MPSS for EMTs to predict the likelihood of performing endovascular therapy after transportation. The rate of endovascular therapy after transportation is obviously higher at CSCs than at PSCs. Patients indicated for endovascular therapy can be transported either to PSCs or CSCs as per the current transfer protocol for implementation of iv-tPA alone, but it is clear that patients transferred to PSCs cannot receive the benefits of endovascular therapy. The present study found a significant correlation between the MPSS evaluated by EMTs and the rate of endovascular therapy after transportation. Even after adjusting for type of stroke center and onset-to-door



**Fig. 2.** Endovascular therapy performed in six primary stroke centers and six comprehensive stroke centers in Kawasaki City, Japan, by Maria Prehospital Stroke Scale (MPSS) score.

time by multivariate logistic regression analysis, MPSS score was found to be an independent predictor for performance of endovascular therapy after transportation.

New prehospital triage and transfer protocols that follow guidelines for endovascular therapy must be explored. However, not enough research has been undertaken on this topic. Protocols tailored to the circumstances of each geographical area should be adopted, either considering the size of the area that the EMTs cover or the varying numbers of PSCs and CSCs that exist in the area. The MPSS, which can predict the performance of endovascular therapy after transportation, may become a new tool offering a flexible solution for each area.

The difference between the MPSS and CPSS is that the MPSS takes into account the severity of deficits in a patient with suspected stroke. Emergency medical technicians might be able to more accurately identify candidates for post-transportation endovascular therapy by adding the full evaluation of the NIHSS to the CPSS or the MPSS. However, the present study did not find any improvement in the diagnostic accuracy for predicting endovascular therapy when the NIHSS score was used as an alternative to the MPSS score, implying that this triage method is impractical and may in fact be a waste of time.

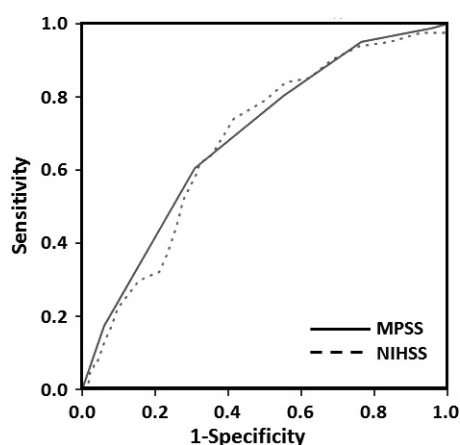
Diagnostic imaging in the acute phase, including evaluation of middle cerebral artery occlusion by computed tomography angiography or magnetic resonance angiography, is the most accurate method of predicting indication for endovascular therapy. Endovascular therapy carried out at PSCs in the present study was limited to cases of onset-to-door time of less than 120 min, whereas endovascular therapy undertaken at CSCs included patients with onset-to-door time of up to 300 min. This implies that CSCs have an endovascular therapist on standby and that CSCs can offer endovascular therapy 24 h a day, 7 days a week with a shorter door-to-puncture time than PSCs. A system could therefore be established where patients transported with prenotification from EMTs of an MPSS  $\geq 3$  are immediately checked for vascular occlusion at a PSC, and then transferred to a CSC in an onset-to-door time of less than 300 min. Telestroke may facilitate this cooperative effort.

The present study had several limitations. First, the Merci Retriever was approved in April 2010 in Japan, the Penumbra System in June 2011, the Trevo Pro Retriever in December 2013, and the Solitaire Flow Restoration device in May 2014. However, the current monitoring system did not record which of these devices was used in endovascular therapy. While differences in patient outcomes could be revealed based on which device was used, the present study only looked into whether endovascular therapy was

**Table 2.** Logistic regression analysis for the prediction of endovascular therapy after admission

	Univariate			Multivariate		
	OR	95% CI	P-value	OR	95% CI	P-value
Male sex	0.945	0.633–1.409	0.781			
Age	1.010	0.995–1.026	0.178			
MPSS score			0.000			0.000
MPSS = 1	1	Reference		1	Reference	
MPSS = 2	2.674	1.035–6.910	0.042	2.386	0.912–6.247	0.076
MPSS = 3	3.606	1.452–8.957	0.006	2.914	1.152–7.372	0.024
MPSS = 4	5.584	2.363–13.200	0.000	5.474	2.300–13.029	0.000
MPSS = 5	11.444	4.453–29.411	0.000	11.459	4.334–30.296	0.000
Type of stroke center			0.000			0.000
Primary stroke center		Reference			Reference	
Comprehensive stroke center	4.478	2.247–8.924	0.000	4.860	2.334–10.148	0.000
Detection-to-door time	0.989	0.967–1.012	0.347			
Onset-to-door time	0.999	0.998–1.000	0.037	0.999	0.999–1.000	0.106

CI, confidence interval; MPSS, Maria Prehospital Stroke Scale; OR, odds ratio.



**Fig. 3.** Receiver–operating characteristic (ROC) curves for predicting endovascular therapy by Maria Prehospital Stroke Scale (MPSS) score and National Institutes of Health Stroke Scale (NIHSS) score. Area under the ROC curve by MPSS score (solid line) and NIHSS score (dotted line) is 0.689 (95% confidence interval, 0.627–0.751) and 0.678 (95% confidence interval, 0.616–0.740), respectively.

undertaken after transportation. Differences in the devices therefore had no effect on the present results. Second, diagnostic accuracy of the MPSS score for predicting endovascular therapy (0.689; 95% CI, 0.627–0.751) is not enough to transport all patients with higher MPSS to hospitals capable of performing endovascular therapy. Further studies are necessary to devise additional information to MPSS, such as signs of conjugate deviation or hemispatial neglect, to

increase the likelihood ratio of this prehospital scale. Finally, indications for iv-tPA therapy are different from those for endovascular therapy, especially in terms of the time window, site of vascular occlusion, mechanism of vascular occlusion, or severity of deficits. It is necessary to explore whether the factors associated with the predictive value of the MPSS score differ between the iv-tPA and endovascular therapies in patients.

## CONCLUSIONS

THE MPSS, WHICH was developed as a tool to predict the performance of iv-tPA therapy after transportation, is useful to EMTs in predicting the performance of endovascular therapy after transportation. Important data can also be obtained for designing transportation protocols within a region.

## CONFLICT OF INTEREST

NONE.

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