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The influence of prestroke disability on outcome in patients with a low Alberta Stroke Program Early CT Score who underwent endovascular thrombectomy

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OBJECTIVE The definitive influence of prestroke disability on outcomes in patients with a low Alberta Stroke Program Early CT Score (ASPECTS) treated with endovascular thrombectomy (EVT) for acute ischemic stroke (AIS) due to large-

ABBREVIATIONS AIS = acute ischemic stroke; ASPECTS = Alberta Stroke Program Early CT Score; EVT = endovascular thrombectomy; LVO = large-vessel occlusion; mRS = modified Rankin Scale; NIHSS = National Institutes of Health Stroke Scale; STAR = Stroke Thrombectomy and Aneurysm Registry.

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vessel occlusion (LVO) remains unknown. This study aimed to investigate the impact of prestroke disability on outcomes in this specific population.

METHODS Data from 32 international centers for AIS-LVO patients with a low ASPECTS who underwent EVT between January 2013 and December 2022 were analyzed retrospectively. Low ASPECTS and prestroke disability were defined as ASPECTS values of 2–5 and prestroke modified Rankin Scale (mRS) score ≥ 2. The primary outcome was a return to the prestroke mRS score at 90 days. Secondary outcomes were independent ambulation (mRS scores of 0–3) or a return to the prestroke mRS score at 90 days, good functional outcome (mRS scores of 0–2) or a return to the prestroke mRS score at 90 days, successful recanalization, and 90-day mortality. Safety outcomes were any intracranial hemorrhage or symptomatic intracranial hemorrhage. A symptomatic intracranial hemorrhage was defined as an intracranial hemorrhage with an associated worsening of ≥ 4 points in the National Institutes of Health Stroke Scale score. Outcomes were compared between patients with and without prestroke disability.

RESULTS Of 293 patients, 50 (17.1%) had a prestroke disability. Of 50 patients, 20 (40.0%), 24 (48.0%), and 6 (12.0%) had prestroke mRS scores of 2, 3, and 4, respectively. The primary outcome showed no significant difference between the two groups. Compared with patients without prestroke disability, those with prestroke disability had a significantly smaller proportion of independent ambulation or return to prestroke mRS score (adjusted OR 0.13, 95% CI 0.03–0.53) and good functional outcome or return to prestroke mRS score (adjusted OR 0.21, 95% CI 0.05–0.91). Other secondary and safety outcomes showed no significant difference between the two groups.

CONCLUSIONS The present study indicated that prestroke disability was not associated with a return to the prestroke mRS score at 90 days or intracranial hemorrhage. Physicians should not routinely exclude AIS-LVO patients with a low ASPECTS who have prestroke disability from EVT based on prestroke disability alone.

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KEYWORDS acute ischemic stroke; endovascular thrombectomy; large-vessel occlusion; low Alberta Stroke Program Early CT Score; prestroke disability; outcomes; vascular disorders

Acute ischemic stroke (AIS) caused by large-vessel occlusion (LVO) is one of the leading causes of death and disability worldwide.[1,2] Recently, the results of four randomized controlled trials suggested that endovascular thrombectomy (EVT) is associated with better functional outcomes in AIS-LVO patients presenting with a low Alberta Stroke Program Early CT Score (ASPECTS).[3–6] The American Heart Association/American Stroke Association guidelines recommend offering EVT to AIS-LVO patients without prestroke disability (defined as a modified Rankin Scale [mRS] score > 1).[7] Consequently, patients with prestroke disability were excluded from these randomized clinical trials.

The mRS is a widely accepted tool to assess disability after AIS.[8] Because many patients with AIS already had prestroke disability, there is now increasing interest in the use of prestroke disability assessed by the mRS as a prognostic tool for AIS outcomes.[9] In this regard, although some studies have demonstrated that prestroke mRS score had no association with accumulated disability but was associated with absolute 90-day disability in AIS-LVO patients with EVT,[10,11] other studies have indicated that prestroke disability was associated with poor outcomes.[12–14]

To date, the impact of prestroke disability on outcomes for AIS-LVO patients with a low ASPECTS undergoing EVT is still undefined. This study aimed to investigate the impact of prestroke disability on outcomes for AIS-LVO patients with a low ASPECTS undergoing EVT using data from an ongoing international multicenter registry.

Methods

We retrospectively reviewed data from the Stroke Thrombectomy and Aneurysm Registry (STAR) for AIS patients with a low ASPECTS (defined as ASPECTS values of 2–5) who underwent EVT for LVO at 32 thrombectomy centers between January 2013 and December 2022. AIS patients with a low ASPECTS who underwent EVT for occlusion of the internal carotid artery and/or M1 segment of the middle cerebral artery were included. EVT decisions were at the discretion of a vascular neurologist and neurointerventionalist on a case-by-case basis. The study was approved by the institutional review board at each individual institution and follows the guidelines set forth by the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.[15] Patient consent to have their data included in the registry and individual studies was waived by the institutional review boards. The data were obtained retrospectively and collected according to a standardized protocol. Verification, de-identification, and attestation of data accuracy were performed by investigators at each contributing institution. Individual patient data from each contributing institution were pooled by STAR investigators.

Clinical data were obtained from the STAR dataset, including age, sex, race/ethnicity, medical history (hypertension, diabetes mellitus, atrial fibrillation, and hyperlipidemia), and prestroke mRS score.[16] Prestroke disability was defined as prestroke mRS scores of 2–4.[10] The prestroke mRS score was evaluated by interviews with the patients and/or family members. The following data were also collected: National Institutes of Health Stroke Scale (NIHSS) score at admission,[17] ASPECTS, primary occluded vessel location, use of intravenous and intra-arterial tissue-type plasminogen activator, onset to arterial puncture time, procedure time, successful recanalization as defined by postprocedure modified Thrombolysis in Cerebral Infarction score ≥ 2b,[18,19] type of EVT procedure, 90-day mRS score, any intracranial hemorrhage, and symptomatic intracranial hemorrhage. Symptomatic intracranial hemor-

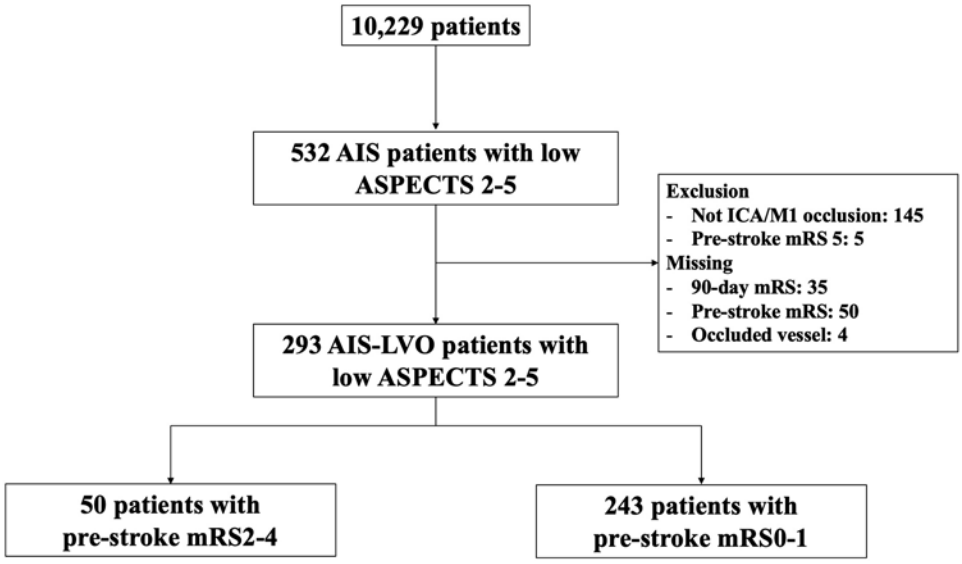

FIG. 1. Study flowchart. ICA = internal carotid artery; M1 = M1 segment of the middle cerebral artery.

rhage was defined as an intracranial hemorrhage with an associated worsening of ≥ 4 points in NIHSS score.[20] The 90-day mRS score was evaluated by telephone interviews with the patient or family members or during a physical examination in those who were able to visit our hospital.

Outcomes

The primary outcome was a return to the prestroke mRS score at 90 days. Secondary outcomes were independent ambulation (90-day mRS scores of 0–3) or a return to the prestroke mRS score at 90 days, good functional outcome (mRS scores of 0–2) or a return to the prestroke mRS score at 90 days, successful recanalization, and 90-day mortality. Safety outcomes were defined as any intracranial hemorrhage or symptomatic intracranial hemorrhage.

Statistical Analysis

Categorical variables are presented as number and percentage and were compared using the chi-square test. Continuous variables are expressed as median and interquartile range and were compared using the Wilcoxon rank-sum test. We presented the number of cases for which data were available.

Baseline and periprocedural characteristics were compared between patients with and without prestroke disability (prestroke mRS scores of 0–1 vs 2–4). Results are shown unadjusted and adjusted for treatment year, age, sex, prior stroke, intravenous thrombolysis, NIHSS score at admission, ASPECTS, primary occluded vessel location, and AIS onset to arterial puncture time.[21–23] As the period of the registry was long and there were significant advances and changes to patient selection, relationships between year and age, prestroke mRS score, NIHSS score at admission, and onset to arterial puncture time were also investigated by simple regression analysis. All statistical analyses were performed using JMP Pro (version 16.0, SAS Institute). Differences were considered significant at a p value < 0.05.

Results

Between January 2013 and December 2022, 10,229 AIS patients treated with EVT were identified. Of these, 293 patients met our inclusion criteria (Fig. 1), with 50 (17.1%) of the included patients having prestroke disability. Of 50 patients, 20 (40.0%), 24 (48.0%), and 6 (12.0%) had prestroke mRS scores of 2, 3, and 4, respectively (Table 1). The median age was 69.0 years (IQR 60.0–78.0 years), and 137 (46.8%) patients were female. In total, 126 (49.0%) patients were White, 30 (11.7%) were Black, 6 (2.3%) were Hispanic, and 95 (37.0%) were other race/ethnicity. The median NIHSS score at admission was 19 (IQR 14–22), and intravenous thrombolysis was used in 99 (33.8%) patients. The median ASPECTS was 5 (IQR 4–5), and the median onset to puncture time was 322 minutes (IQR 204–618 minutes). Patients with prestroke disability were older (77.0 vs 67.0 years, $p < 0.001$), had a higher proportion of prior stroke (26.0% vs 10.3%, $p < 0.003$), had a higher median NIHSS score at admission (21 vs 18, $p = 0.002$), and had a shorter onset to puncture time (244 vs 340 minutes, $p = 0.043$) (Table 1). Other baseline characteristics and all procedural characteristics showed no significant difference between the two groups.

Outcomes

Distributions of prestroke and 90-day mRS scores are shown in Fig. 2. A return to the prestroke mRS score at 90 days was observed in 11 of 207 (5.3%) patients with a prestroke mRS score of 0, 3 of 36 (8.3%) with a prestroke mRS score of 1, 1 of 20 (5.0%) with a prestroke mRS score of 2, 3 of 24 (12.5%) with a prestroke mRS score of 3, and 0 of 6 (0%) patients with a prestroke mRS score of 4. The proportion of patients with prestroke disability as the primary outcome compared with those without showed no significant difference (Table 2). Patients with prestroke disability were less likely to have independent ambulation or a return to their prestroke mRS score at 90 days (10.0%

TABLE 1. Baseline and procedural characteristics between patients with ASPECTS values of 2–5 by prestroke disability

	Total (n = 293)	Prestroke Disability		p Value
		Yes (n = 50)	No (n = 243)	
Baseline characteristics				
Age, yrs	69.0 (60.0–78.0)	77.0 (65.8–84.1)	67.0 (58.5–76.0)	<0.001
Female sex	137 (46.8)	23 (46.0)	114 (46.9)	0.91
Race/ethnicity (n = 257)				0.57
White	126 (49.0)	24 (55.8)	102 (47.7)	
Black	30 (11.7)	4 (9.3)	26 (12.1)	
Hispanic	6 (2.3)	0	6 (2.8)	
Other	95 (37.0)	15 (34.9)	80 (37.4)	
Current smoker	34 (11.6)	4 (8.0)	30 (12.3)	0.38
Prestroke mRS score				<0.001
0	207 (70.6)	0	207 (85.2)	
1	36 (12.3)	0	36 (14.8)	
2	20 (6.8)	20 (40.0)	0	
3	24 (8.2)	24 (48.0)	0	
4	6 (2.0)	6 (12.0)	0	
Hypertension	205 (70.0)	37 (74.0)	168 (69.1)	0.49
Diabetes mellitus	89 (30.4)	18 (36.0)	71 (29.2)	0.34
Atrial fibrillation	107 (36.5)	21 (42.0)	86 (35.4)	0.38
Dyslipidemia	109 (37.2)	17 (34.0)	92 (37.9)	0.61
Prior stroke	38 (13.0)	13 (26.0)	25 (10.3)	0.003
Admission NIHSS score	19 (14–22)	21 (17–25)	18 (14–22)	0.002
Intravenous thrombolysis	99 (33.8)	18 (36.0)	81 (33.3)	0.72
Occluded vessel				0.40
ICA	85 (29.0)	16 (32.0)	69 (28.4)	
M1 segment of MCA	167 (57.0)	30 (60.0)	137 (56.4)	
ICA & M1 segment of MCA	41 (14.0)	4 (8.0)	37 (15.2)	
ASPECTS	5 (4–5)	5 (4–5)	5 (4–5)	0.75
Procedural characteristics				
Onset to puncture time, mins	322 (204–618)	244 (175–478)	340 (219–642)	0.043
Procedure time, mins	47 (21–76)	38 (20–70)	40 (21–72)	0.95
No. of thrombectomy attempts	2 (1–3)	2 (1–3)	2 (1–3)	0.71
Intra-arterial thrombolysis (n = 291)	6 (2.1)	1 (2.0)	5 (2.1)	0.97
Mechanical thrombectomy technique (n = 245)				0.82
Aspiration	172 (70.2)	31 (72.1)	141 (69.8)	
Stent retriever	42 (17.1)	8 (18.6)	34 (16.8)	
Combined	28 (11.4)	4 (9.3)	24 (11.9)	
Other	3 (1.2)	0	3 (1.5)	

ICA = internal carotid artery; MCA = middle cerebral artery.
Values are expressed as number of patients (%) or median (IQR) unless otherwise indicated.

vs 40.7%) (unadjusted OR 0.16, 95% CI 0.06–0.42; adjusted OR 0.13, 95% CI 0.03–0.53) (Table 2). Those with prestroke disability were less likely to have a good functional outcome or return to their prestroke mRS score at 90 days (8.0% vs 24.7%) (unadjusted OR 0.27, 95% CI 0.09–0.77; adjusted OR 0.21, 95% CI 0.05–0.91). Those with prestroke disability were more likely to have a 90-day mortality in the unadjusted model (52.0% vs 28.0%) (OR 2.79, 95% CI 1.50–5.19), but this difference showed no significance in the adjusted model (OR 1.80, 95% CI 0.77–4.21). Other secondary and safety outcomes showed no significant differences between the two groups (Table 2).

Simple regression analysis showed no significant associations between treatment year and age, prestroke mRS score, NIHSS score at admission, and onset to arterial puncture time (Fig. 3).

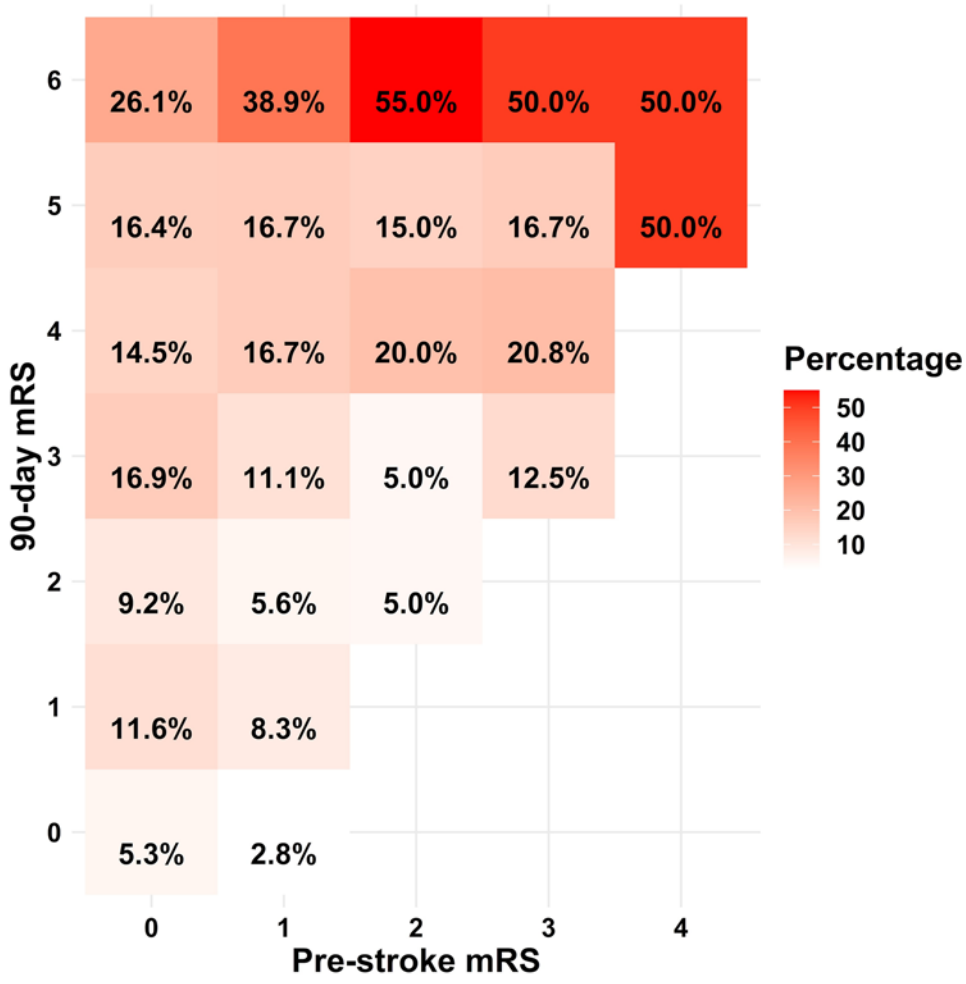

FIG. 2. Distribution of patients with ASPECTS values of 2–5 by prestroke and 90-day mRS scores. Figure is available in color online only.

TABLE 2. Outcomes of patients with and without prestroke disability

	Total (n = 293)	Prestroke Disability		Unadjusted		Adjusted	
		Yes (n = 50)	No (n = 243)	OR (95% CI)	p Value	OR (95% CI)	p Value
Primary outcome							
Return to prestroke mRS score	18 (6.1)	4 (8.0)	14 (5.8)	1.42 (0.45–4.52)	0.55	2.52 (0.43–14.8)	0.31
Secondary outcome							
Return to prestroke mRS score or mRS scores of 0–3	104 (35.5)	5 (10.0)	99 (40.7)	0.16 (0.06–0.42)	<0.001	0.13 (0.03–0.53)	0.004
Return to prestroke mRS score or mRS scores of 0–2	64 (21.8)	4 (8.0)	60 (24.7)	0.27 (0.09–0.77)	0.01	0.21 (0.05–0.91)	0.04
Successful recanalization (n = 288)	233 (80.9)	37 (74.0)	196 (82.4)	0.61 (0.30–1.25)	0.17	0.64 (0.25–1.68)	0.37
90-day mortality	94 (32.1)	26 (52.0)	68 (28.0)	2.79 (1.50–5.19)	0.001	1.80 (0.77–4.21)	0.18
Safety (n = 291)							
Any intracranial hemorrhage	115 (39.5)	22 (45.8)	93 (38.3)	1.36 (0.73–2.55)	0.33	1.62 (0.73–3.58)	0.25
Symptomatic intracranial hemorrhage	43 (14.8)	10 (20.8)	33 (13.6)	1.62 (0.74–3.56)	0.23	2.16 (0.76–6.19)	0.15

Values are expressed as number of patients (%) unless otherwise indicated.

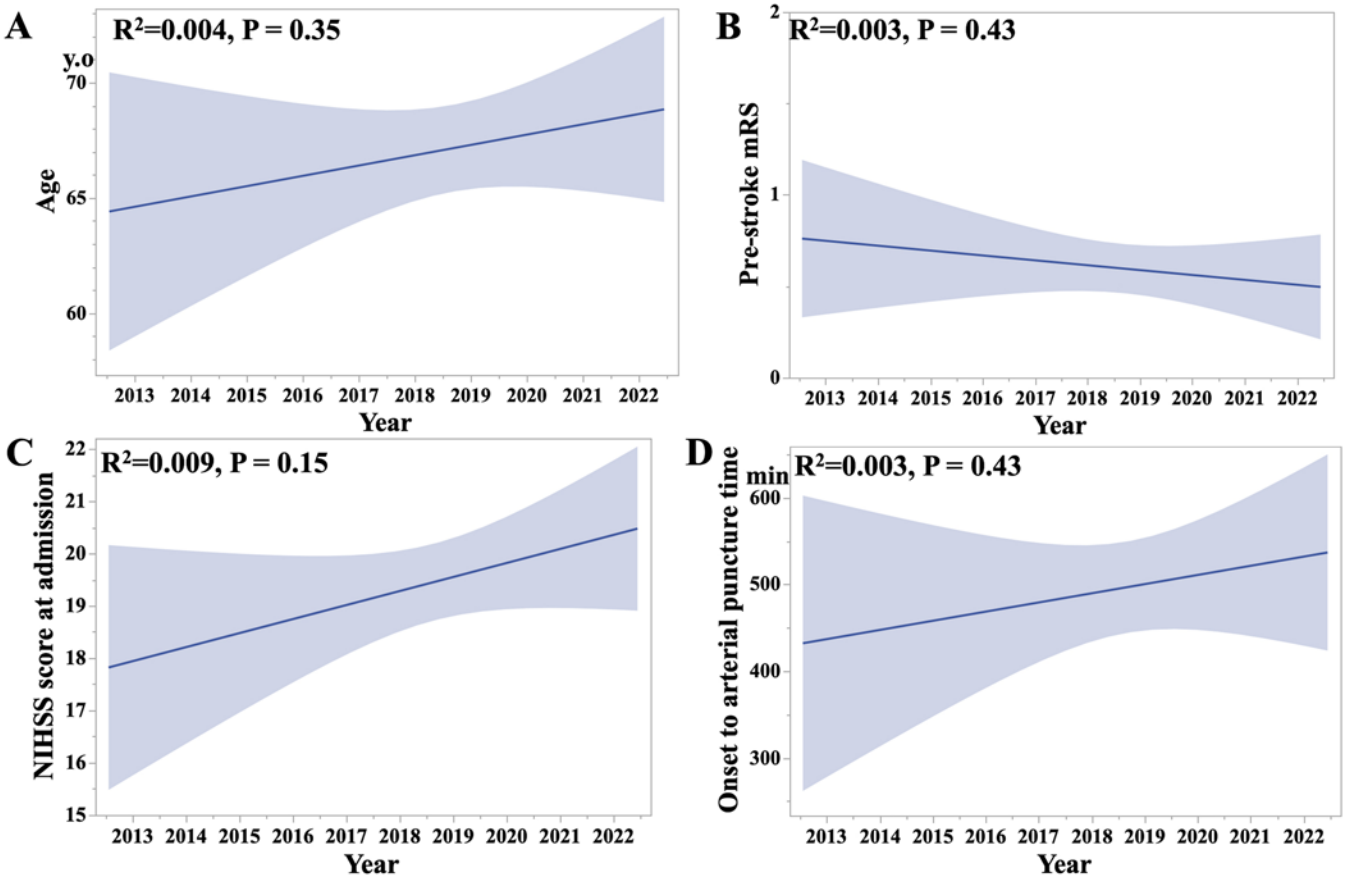

FIG. 3. Relationships between treatment year and age (**A**), prestroke mRS score (**B**), NIHSS score at admission (**C**), and onset to arterial puncture time (**D**). Figure is available in color online only.

Discussion

The present study showed that prestroke disability was not related to a return to prestroke mRS score at 90 days in AIS-LVO patients with a low ASPECTS who underwent EVT. It also showed that prestroke disability was not related to successful recanalization, 90-day mortality, or any intracranial hemorrhage or symptomatic intracranial hemorrhage.

A previous population-based study showed that AIS patients with prestroke disability treated with optimum medical treatment had higher mortality, institutionalization, and costs if they accumulated additional disability due to AIS.[24] In addition, another study indicated that patients with moderately severe prestroke disability (defined as an mRS score of 4) had poorer outcomes compared with those with moderate prestroke disability (defined as an mRS score of 3), and about 20% of patients returned to their prestroke mRS score.[12] On the other hand, prestroke disability did not detract from the relative benefit of EVT evaluated as accumulated disability and was not associated with procedural complications in a prior study.[10] Other studies showed that prestroke disability did not influence successful recanalization, intracranial hemorrhage, or return to prestroke functional level, although it was related to 90-day mortality.[13,14] These studies included patients with a low ASPECTS as well as those with a nonlow ASPECTS and suggested that physicians should not routinely exclude patients harboring prestroke disability from EVT for AIS-LVO. Similar to these studies, our analysis demonstrated that prestroke disability itself was not associated with a return to prestroke mRS score at 90 days in AIS-LVO patients with a low ASPECTS who underwent EVT.

There are some ethical issues to consider when performing EVT for AIS-LVO patients with prestroke disability, as extending survival comes at the price of living longer with a severe disability, and possibly being bedridden if a worsening of the mRS score ensues. In this regard, no patients with a prestroke mRS score of 4 had a 90-day mRS score of 4, and all of them had a 90-day mRS score of 5 or 6 in the present study. However, even among patients with prestroke mRS scores of 1, 2, and 3, 72.2%, 90.0%, and 87.5%, respectively, had mRS scores of 4–6 at 90 days. Although the proportions of patients with independent ambulation or a return to prestroke mRS score and patients with a good functional outcome or a return to prestroke mRS score at 90 days were higher for those without prestroke disability, this was not surprising, as patients with prestroke disability would never have an outcome better than their prestroke mRS score. Therefore, physicians should consider whether to perform EVT for AIS-LVO patients with a low ASPECTS based not only on prestroke disability but also on other factors that could affect the outcome.

In the present study, patients with prestroke disability were older, had a higher admission NIHSS score, had a higher proportion of prior stroke, and had a shorter onset to puncture time than those without prestroke disability, while all other demographic and procedural metrics were similar between the two groups. These results could be due to the onset of AIS could being detected earlier by family members or caregivers. Although older age and higher admission NIHSS score could affect outcomes, our results indicated that prestroke disability was not related to a return to prestroke mRS score at 90 days even after adjustment of these factors. Contrary to patients with a nonlow ASPECTS, those with a low ASPECTS are more likely to sustain significant cortical region damage and substantial core infarct.[25] Regardless of these factors that seem to be dominant in patients with a low ASPECTS, the negative influence of prestroke disability on EVT outcomes may not be greater in this specific population.

Limitations

This study has several limitations. First, as the registry did not capture patients treated only with medical management, the impact of prestroke disability on outcome could be only described in AIS-LVO patients presenting with a low ASPECTS who underwent EVT. Such a study would require comparison with a medical management group to see if there is still a benefit to offering EVT despite the relatively low likelihood of meaningful clinical improvement. Therefore, large, prospective, multicenter, randomized studies are necessary to address this limitation. Second, information regarding the causes of prestroke disability and antithrombotic usage, which might influence outcomes, could not be determined. Third, the retrospective nature of this study could result in selection bias, and the outcomes were not adjudicated by a core laboratory. Fourth, patients with missing variables were excluded from this study. As these excluded patients might influence outcomes, the results should be carefully interpreted. Fifth, the period of the registry was very long, and this may have an influence on outcomes, although treatment years were included in the adjusted model. Finally, while only 6 patients had a prestroke mRS score of 4, none of these patients returned to that level. Unfortunately, we were unable to obtain any additional information on these patients, but it seems somewhat unusual to offer thrombectomy in such patients.

Conclusions

Prestroke disability was not related to a return to prestroke mRS score at 90 days, successful recanalization, 90-day mortality, or any intracranial hemorrhage or symptomatic intracranial hemorrhage in AIS-LVO patients with a low ASPECTS who underwent EVT. Physicians should not routinely exclude AIS-LVO patients with a low ASPECTS who have prestroke disability from EVT based on prestroke disability alone, although careful discussion with the patient and their family is indispensable.

Acknowledgments

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