ORIGINAL RESEARCH

Leptomeningeal Collaterals and Infarct Progression in Patients With Acute Large-Vessel Occlusion and Low NIHSS

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BACKGROUND: Approximately 10% of patients with acute ischemic stroke with large-vessel occlusion (LVO) have mild neurological deficits. Although leptomeningeal collaterals (LMCs) are the major determinant of clinical outcomes for patients with acute ischemic stroke with LVO, the contribution of baseline LMC status to subsequent infarct progression in patients with mild stroke with LVO is poorly defined.

METHODS: This observational study included patients with acute anterior circulation LVO and mild stroke symptoms (National Institutes of Health Stroke Scale < 6) from a prospectively collected, multicenter, national stroke registry. The Alberta Stroke Program Early Computed Tomography Score was quantified on the initial and follow-up images. An infarct progression, defined as any Alberta Stroke Program Early Computed Tomography Score decrease between the initial versus follow-up scans, was categorized as either 0/1/2+. The LMCs on the baseline images were graded as good, fair, or poor.

RESULTS: Of the 623 included patients (mean age, 67.6±13.4 years; 380 [61.0%] men; 186 [29.9%] with reperfusion treatment), the baseline LMC was graded as good in 331 (53.1%), fair in 219 (35.2%), and poor in 73 (11.7%). The Alberta Stroke Program Early Computed Tomography Score decrement was noted as 0 in 288 (46%) patients, 1 in 154 (24%), and 2+ in 181 (29%). A poor LMC was associated with an infarct progression (adjusted odds ratio, 2.05 [95% CI, 1.22–3.47]).

CONCLUSIONS: Poor collateral blood flow was associated with infarct progression in patients with acute ischemic stroke with LVO and mild symptoms. In this selective population, early assessment of collateral blood flow status can help in early detection of patients susceptible to infarct progression.

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Immediately after emergent large-vessel occlusion (LVO) occurs, irreversible ischemic injury propagates over the affected vascular territory.[1] Successful revascularization is considered the only effective option to save the intact brain.[2–6] Most clinical guidelines recommend initiating intravenous thrombolysis or endovascular treatment (EVT) within a fixed time window to maximize their treatment effects.[7,8] As there are individual variabilities in the recruitment of leptomeningeal collateral (LMC) and collateral perfusion to the ischemic brain, baseline LMC perfusion is an important determinant of outcomes in patients who are candidates for recanalization treatment.[9–11]

The role of the LMC has not been established in patients with LVO with mild neurological deficits, who comprise ≈10% of the patients who have acute ischemic strokes from LVO.[12] Due to the exclusion from randomized clinical trials, the efficacy of EVT for such patients has not been tested and should await current ongoing trials (MOSTE [Minor Stroke Therapy Evaluation; NCT03796468] and ENDOLOW [Endovascular Therapy for Low NIHSS Ischemic Strokes; NCT04167527]). The currently available data from the previous observational studies have reported conflicting results on the effectiveness of EVT for patients with mild LVO.[13–15] Considering these patients' milder neurological deficits, it may be reasonable to wait and see whether their irreversible ischemia progresses during their in-hospital care. However, it is known that 10%–20% of patients with mild LVO experience early neurological deterioration (END) and end up having poor functional outcomes.[16] Thus, it is imperative to identify patients with mild LVO with a higher likelihood of ischemic lesion and symptom progression to improve functional outcomes.

The authors hypothesized that the extent of LMC might be inversely correlated with the infarct progression in patients with acute LVO with a mild neurological symptom at baseline. We analyzed the clinical and imaging data that were collected from a multicenter acute stroke registry to investigate the contribution of the baseline LMC to the imaging and clinical outcomes.

METHODS

Patient Selection

Between January 1, 2015, and March 31, 2019, 36 339 patients who were admitted with acute ischemic stroke and transient ischemic attack were screened from a prospectively collected, ongoing, nationwide, multicenter acute stroke registry (CRCS-K [Clinical Research Collaboration for Stroke in Korea] registry).[17] Patients with acute stroke with the following criteria were included: (1) arrived <24 hours from the time last known well (n=24 596), (2) a baseline National Institutes of Health Stroke Scale (NIHSS) score <6 points (n=15 436), (3) anterior circulation LVO (interior carotid artery [ICA] or M1 or proximal M2 segment of the middle cerebral artery) confirmed by neuroimaging (n=1083), (4) follow-up brain computed tomography (CT) or magnetic resonance scans available (n=676), and (5) baseline images are suitable for collateral evaluation (n=623; Figure 1). The patients were managed by the institutional protocols based on the national guidelines at the time of treatment and at the discretion of the attending vascular neurologists. Although imaging protocols for acute ischemic stroke have not been standardized across centers, CT was the preferred initial image when patients arrived at the hospital within the time window of intravenous thrombolysis. Otherwise, magnetic resonance imaging was preferred where possible. The local institutional review boards of all participating centers of the CRCS-K registry approved the study with a waiver of consent. The secondary use of the registry data and additional review of medical records for this study were approved by the institutional review board of Seoul National University Bundang Hospital (B-2007-622-105).

Data Collection and Definition

The clinical data, including demographics, vascular risk factors, and stroke characteristics, were retrieved from the CRCS-K registry.[17]

The imaging data were retrospectively obtained and evaluated by a central image core lab, which consisted of 6 vascular neurologists (J.H.H., B.J.K., B.J.K., C.K.K., and J.-T.K.), 3 interventional neurologists (J.G.K., H.P., and J.S.Y.), and 1 interventional radiologist (S.H.B.). More than 2 of these raters evaluated the brain images while being blinded to the patient's clinical information involved with each image (for interrater agreement of image readings, see Table S1). Any discrepancies between the raters were resolved by an independent panel (B.J.K., J.S.Y., and S.H.B.).

The Alberta Stroke Program Early CT Score (ASPECTS) of the baseline and follow-up neuroimaging images were assessed using CT scans and diffusion-weighted imaging (DWI)–magnetic resonance imaging

images.[18] ASPECTS using DWI–magnetic resonance imaging was counted as positive when acute ischemic lesions in DWI exceeded one-third of the corresponding ASPECTS standard template. A follow-up image that was closest to 96 hours (range, 36–120 hours) from the baseline was selected; those with the same modality as the baseline were preferentially selected. Infarct progression, represented by ASPECTS decrement, was defined as any decrease in the second ASPECTS compared with the baseline. The infarct progression was also categorized as an ASPECTS decrement of 0 (no change), 1, or 2+.

The occlusion location and LMC status were assessed using the initial images taken within 24 hours from the admission of the patient in the following order of selection: pretreatment digital subtraction angiography, single- or multiphase CT angiography, and time-of-flight magnetic resonance angiography.[19] Occlusion location was categorized as extracranial ICA (C1 segment of ICA), intracranial ICA (C2–C7 segment of ICA), M1 (distal to C7 of ICA to middle cerebral artery bifurcation/trifurcation), and M2 (distal to middle cerebral artery bifurcation/trifurcation).[20] The pial arterial filling score was used for grading the CT angiography and magnetic resonance angiography collateral flow status, and the American Society of Interventional and Therapeutic Neuroradiology/Society of Interventional Radiology scoring system was used for evaluating the digital subtraction angiography.[21,22] The LMC status was evaluated by digital subtraction angiography in 152 patients (24%), by CT angiography in 137 (22%), and by time-of-flight magnetic resonance angiography in 334 patients (54%). The LMC status was categorized as good (pial arterial filling score of 4, 5; and American Society of Interventional and Therapeutic Neuroradiology/Society of Interventional Radiology grade 3, 4), fair (filling score of 2, 3; and American Society of Interventional and Therapeutic Neuroradiology/Society of Interventional Radiology grade 2), or poor (filling score of 0, 1 and American Society of Interventional and Therapeutic Neuroradiology/Society of Interventional Radiology grade 0, 1) for the analyses.

END due to the index stroke was defined when ≥1 of the following conditions were met: a total NIHSS increase of ≥2, an NIHSS level of consciousness subscore (1a, 1b, or 1c), or a motor subscore (5a, 5b, 6a, or 6b) increase of ≥1.[23]

Statistical Analysis

The baseline characteristics of the included patients were compared and summarized using χ^2 tests for the categorical variables and t tests for the continuous variables. The association between the LMC grades (good, fair, and poor) and the infarct progression was investi-

Nonstandard Abbreviations and Acronyms

ASPECTS	Alberta Stroke Program Early Computed Tomography Score
CRCS-K	Clinical Research Collaboration for Stroke in Korea
DWI	diffusion-weighted imaging
END	early neurological deterioration
EVT	endovascular treatment
ICA	interior carotid artery
LMC	leptomeningeal collateral
LVO	large-vessel occlusion

CLINICAL PERSPECTIVE

What Is New?

- In patients with mild stroke with large-vessel occlusion, poor leptomeningeal collateral scores were associated with infarct lesion progression.

What Are the Clinical Implications?

- Assessment of the leptomeningeal collateral score can help predict progression of infarct lesions and select proper candidates for emergent endovascular treatment in patients with large-vessel occlusion and mild stroke symptoms.

gated by ordinal logistic regression models, while using the categorized ASPECTS decrement (0, 1, and 2+) as a dependent variable. The model was adjusted for the covariates that had clinical relevance or a bivariate P value <0.10 (the significant variables included age, sex, presence of atrial fibrillation, time from last known well to arrival, baseline NIHSS, baseline ASPECTS score, type of acute reperfusion treatment, and occluded vessel). Interactions between the LMC grades and subgroup variables (age, sex, hypertension, diabetes, atrial fibrillation, acute reperfusion treatment, and occlusion site) on the infarct progression were tested. As a sensitivity analysis, a multivariable Poisson regression model was constructed, after adjusting for overdispersion and by using the uncategorized ASPECTS decrement (range, 0–10) as a dependent variable. The role of the LMC grades in the clinical deterioration was further tested for associations with the occurrence of END and NIHSS score in END cases. The statistical significance level was set at a P value of <0.05 using 2-tailed tests. The
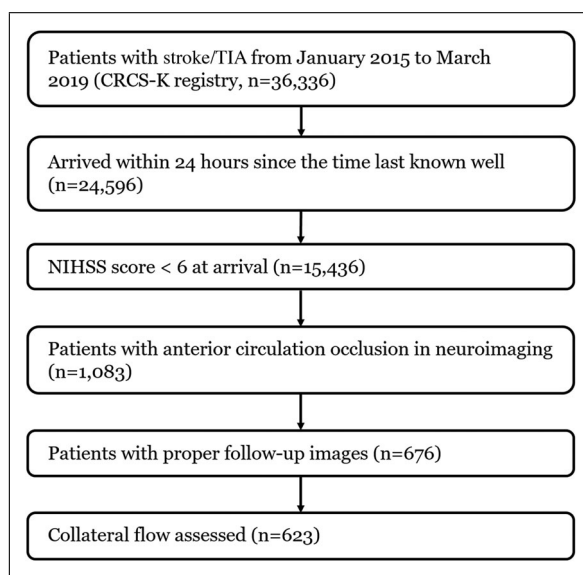
Figure 1.   Study flowchart.
CRCS-K indicates Clinical Research Centre for Stroke–Korea; NIHSS, National Institutes of Health Stroke Scale; and TIA, transient ischemic attack.

significance levels of the interaction terms were adjusted for the subgroup analyses at a P value level of <0.10.[24] The statistical analyses were performed using R version 4.0.3 (R Development Core Team, Vienna, Austria).

RESULTS

Patient Characteristics

A total of 623 patients with acute LVO with baseline NIHSS scores of <6 were included in this study. The mean age of the patients was 67.6±13.4 years, 380 (61%) patients were men, and the median baseline NIHSS of the included patients was 2 (interquartile range, 1–4). Of the patients, 60% had hypertension, 29% had diabetes, and 29% had atrial fibrillation. Among the patients, 105 (17%) patients received intravenous thrombolysis, and 119 (19%) patients received EVT. The LMC grade was good in 331 (53%) patients, fair in 219 (35%), and poor in 73 (12%). The median baseline ASPECTS was 10 [interquartile range, 9–10], and the median follow-up ASPECTS was 8.[7–9] The follow-up ASPECTS was measured after a median of 86 hours [interquartile range, 67–96] after the baseline score. An infarct progression was found in 335 (54%) patients, and an ASPECTS decrement of ≥2 was detected in 181 (29%). A dramatic infarct progression, defined as an ASPECTS decrease of ≥6, occurred in 16 (2.6%) patients.

Leptomeningeal Collateral and Infarct Progression in Patients With Mild LVO

The patients with an infarct progression arrived earlier from the last known well, had higher baseline NIHSS scores, and had more frequent revascularization treatment than the patients without an infarct progression (Table 1). A poor LMC grade was more frequently observed in the patients with an infarct progression (17% in ASPECTS decrement 2+; 14% in ASPECTS decrement 1; and 7% in no ASPECTS decrement). The patients with mild LVO with a poor LMC grade showed higher odds of having a greater infarct progression (for fair LMC, adjusted common odds ratio, 1.23 [95% CI, 0.87–1.74]; for poor LMC, adjusted common odds ratio, 2.05 [95% CI, 1.22–3.47]; compared with patients with a good LMC; Table 2, Figure 2, Table S2). The baseline LMC grade was also significantly associated with the continuous raw value of the ASPECTS decrement (for fair LMC, the adjusted risk ratio was 1.07 [95% CI, 0.84–1.34]; for a poor LMC, the adjusted risk ratio was 1.56 [95% CI, 1.15–2.10], compared with a good LMC; Table S3). The effect of the LMC on the infarct progression was modified by hypertension, diabetes, and the occlusion location (Figure 3). The odds ratios for a poor LMC on the infarct progression were mitigated in the subgroup with hypertension, diabetes, or middle cerebral artery occlusion. The association between the baseline LMC and the infarct progression was consistent regardless of the imaging modalities to evaluate the ASPECTS and LMC grades (see the Supplemental Data and Table S4). In both the subgroup of patients whose LMC grades were assessed by CT angiography or digital subtraction angiography and the subgroup assessed by time-of-flight magnetic resonance angiography, lower LMC grades tended to be associated with infarct progression without statistical significance (Table S5). The association between poor LMC grade, infarct progression, and END also maintained in the subgroup of patients who did not receive acute reperfusion treatment (Table S6).

Leptomeningeal Collateral and END in Patients With Mild LVO

END occurred in 152 patients (24%) during in-hospital care. END occurrence was not associated with the LMC grade. The NIHSS score increase in the patients with END showed a significant correlation with the baseline LMC grades; the medians of the NIHSS increase were 3 [1–5.5] in patients with good LMC, 6 [2–10] in fair patients with LMC, and 6 [3–12.5] in poor patients with LMC (P-for-trend <0.01). The associations between the LMC and the increase in the NIHSS score on the

Table 1. Characteristics According to the Infarct Progression

	ASPECTS decay			
	0 (n=288)	1 (n=154)	≥2 (n=181)	P value
Age, y	67.0±14.0	68.2±12.5	68.0±13.2	0.58
Sex, male, n (%)	173 (60.1)	96 (62.3)	111 (61.3)	0.89
LKW to arrival (h)	5.4 (1.9–11.0)	5.3 (2.1–10.4)	2.7 (1.3–5.8)	<0.01
Baseline NIHSS	2 (0–3)	3 (1–4)	3 (1–4)	<0.01
Premorbid mRS 0–1, n (%)	256 (88.9)	134 (87.0)	164 (90.6)	0.58
Vascular risk factor, n (%)				
Hypertension	171 (59.4)	98 (63.6)	105 (58.0)	0.55
Diabetes	85 (29.5)	46 (29.9)	52 (28.7)	0.97
Dyslipidemia	78 (27.1)	39 (25.3)	36 (19.9)	0.21
Smoking	102 (35.4)	59 (38.3)	73 (40.3)	0.55
Atrial fibrillation	69 (24.0)	52 (33.8)	57 (31.5)	0.06
Recanalization treatment, n (%)				
IVT	20 (6.9)	11 (7.1)	36 (19.9)	
EVT	26 (9.0)	23 (14.9)	32 (17.7)	<0.01
IVT+EVT	9 (3.1)	8 (5.2)	21 (11.6)	
Extent of leptomeningeal collateral, n (%)				
Good	168 (58.3)	76 (49.4)	87 (48.1)	
Fair	99 (34.4)	57 (37.0)	63 (34.8)	0.01
Poor	21 (7.3)	21 (13.6)	31 (17.1)	
Occluded artery, n (%)				
Extracranial ICA	82 (28.5)	40 (26.0)	56 (30.9)	0.51
Intracranial ICA	15 (5.2)	7 (4.6)	6 (3.3)	
M1	93 (32.3)	57 (37.0)	71 (39.2)	
M2	98 (34.0)	50 (32.5)	48 (26.5)	
Outcome				
END	30 (10.4)	39 (25.3)	83 (45.9)	<0.01
NIHSS at END	5 (3–8)	6 (4.5–8)	8 (5–14)	<0.01
mRS 0–2 at 3 mo	218 (75.7)	101 (65.6)	92 (50.8)	<0.01

END indicates early neurological deterioration; EVT, endovascular treatment; ICA, internal carotid artery; IVT, intravenous thrombolysis; LKW, last known well; mRS, modified Rankin Scale; and NIHSS, National Institutes of Health Stroke Scale.

Table 2. Multivariable Model for Infarct Progression (Trichotomized ASPECTS Decrement) and END According to Collateral Flow

	Crude OR (95% CI)	P value	Adjusted OR (95% CI)	P value
Infarct progression				
Good collaterals	Reference		Reference	
Fair collaterals	1.21 (0.88–1.66)	0.25	1.23 (0.87–1.74)	0.24
Poor collaterals	2.29 (1.43–3.67)	<0.01	2.05 (1.22–3.47)	<0.01
END				
Good collaterals	Reference		Reference	
Fair collaterals	0.92 (0.61–1.38)	0.69	0.85 (0.54–1.31)	0.45
Poor collaterals	1.56 (0.89–2.69)	0.11	1.16 (0.61–2.15)	0.65

ASPECTS indicates Alberta Stroke Program Early CT Score; END, early neurological deterioration; and OR, odds ratio.

END remained significant in a multivariable model (for a fair LMC, the adjusted risk ratio [95% CI] was 1.68 [1.19–2.38]; for poor collateral, the adjusted risk ratio was 1.99 [1.33–2.95], compared with a good LMC; see Table S7).

DISCUSSION

From 623 patients with acute LVO with mild neurological deficits, we documented a significant association between the extent of the baseline LMC and in-hospital
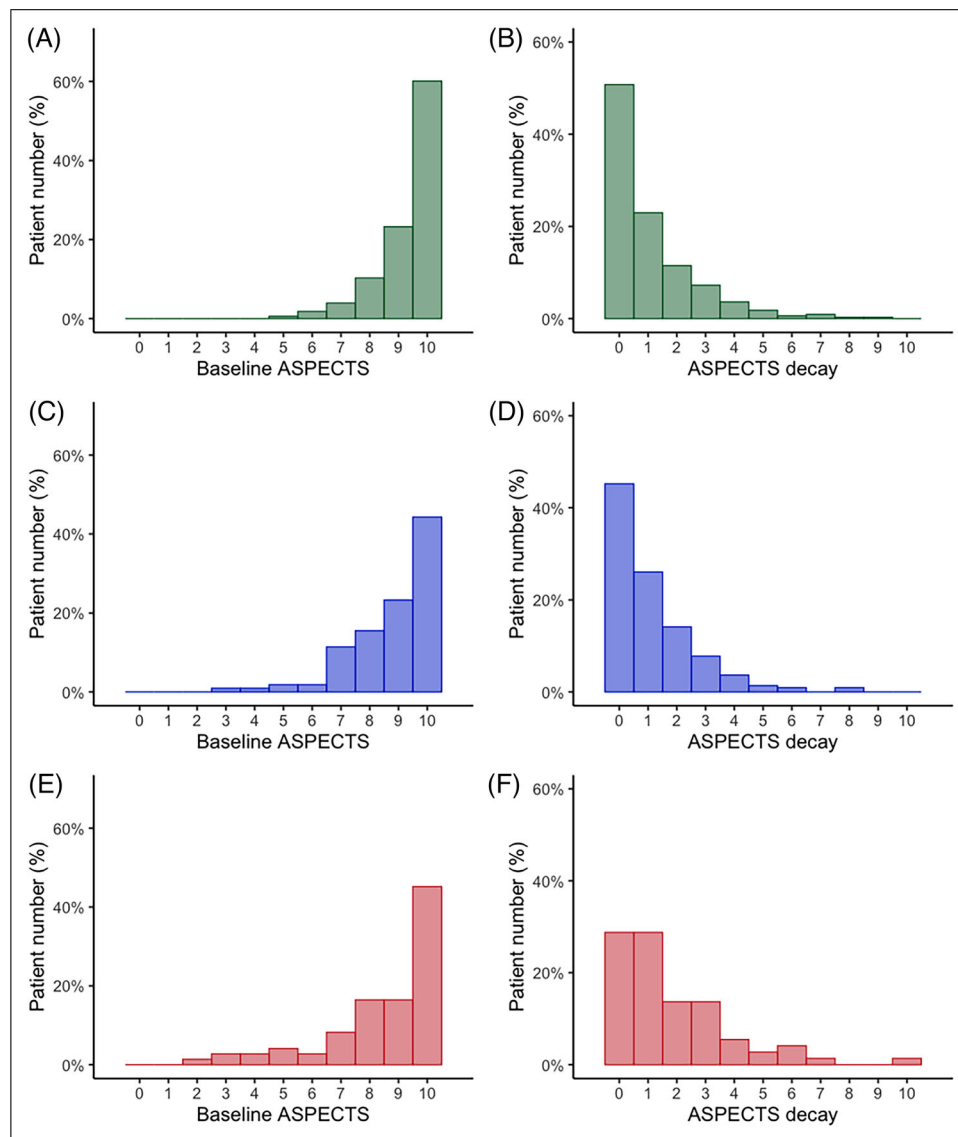
Figure 2. Distribution of baseline ASPECTS and ASPECTS decrement according to collateral blood flow.
A and **B**, Patients with good collateral flow; (**C, D**) patients with fair collateral flow; and (**E, F**) patients with poor collateral flow. ASPECTS indicates Alberta Stroke Program Early Computed Tomography Score.

infarct progression, regardless of acute recanalization treatment. Although END during in-hospital care was not associated with the baseline LMC extent, we found that patients with mild LVO with a poor LMC would experience more prominent neurological deterioration when END occurred.

Approximately half of the patients with mild LVO showed an increase in infarct volume on follow-up brain imaging during in-hospital care. The prognostic indicator for infarct progression among patients with mild LVO has not been widely studied, except for 1 recent study that reported the role of the thrombus length and the occlusion location on clinical deterioration.[25] Our study may provide clinical guidance to consider

evaluating the baseline LMC grade in the in-hospital management to prevent infarct progression. Our findings support that the role of the LMC perfusion is influential after emergent LVO to support the ischemic penumbra, even in patients with mild LVO. Since the LMC perfusion to the ischemic region over the LVO is not supposed to maintain the viability of brain tissue indefinitely, an early assessment of the patient's collateral condition may help to reassess the effectiveness of EVT in patients with minor stroke with LVO in the current era of prolonged EVT time windows.[13,26,27]

Our finding of poor LMC extent in patients with diabetes compared with those without diabetes is consistent with previous literature that demonstrated the
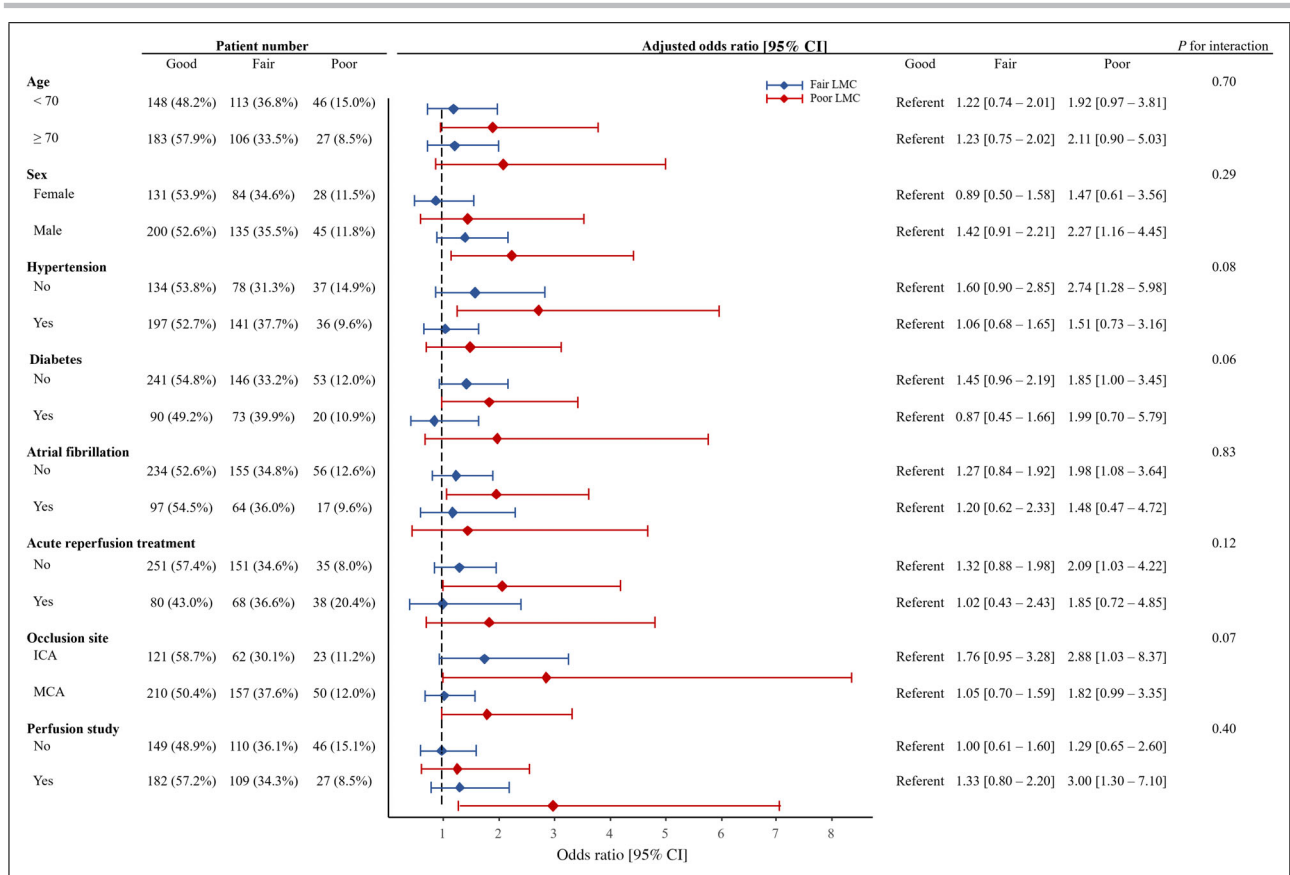
	Patient number			Adjusted odds ratio [95% CI]				P for interaction
	Good	Fair	Poor		Good	Fair	Poor	
Age								0.70
< 70	148 (48.2%)	113 (36.8%)	46 (15.0%)		Referent	1.22 [0.74 – 2.01]	1.92 [0.97 – 3.81]	
≥ 70	183 (57.9%)	106 (33.5%)	27 (8.5%)		Referent	1.23 [0.75 – 2.02]	2.11 [0.90 – 5.03]	
Sex								0.29
Female	131 (53.9%)	84 (34.6%)	28 (11.5%)		Referent	0.89 [0.50 – 1.58]	1.47 [0.61 – 3.56]	
Male	200 (52.6%)	135 (35.5%)	45 (11.8%)		Referent	1.42 [0.91 – 2.21]	2.27 [1.16 – 4.45]	
Hypertension								0.08
No	134 (53.8%)	78 (31.3%)	37 (14.9%)		Referent	1.60 [0.90 – 2.85]	2.74 [1.28 – 5.98]	
Yes	197 (52.7%)	141 (37.7%)	36 (9.6%)		Referent	1.06 [0.68 – 1.65]	1.51 [0.73 – 3.16]	
Diabetes								0.06
No	241 (54.8%)	146 (33.2%)	53 (12.0%)		Referent	1.45 [0.96 – 2.19]	1.85 [1.00 – 3.45]	
Yes	90 (49.2%)	73 (39.9%)	20 (10.9%)		Referent	0.87 [0.45 – 1.66]	1.99 [0.70 – 5.79]	
Atrial fibrillation								0.83
No	234 (52.6%)	155 (34.8%)	56 (12.6%)		Referent	1.27 [0.84 – 1.92]	1.98 [1.08 – 3.64]	
Yes	97 (54.5%)	64 (36.0%)	17 (9.6%)		Referent	1.20 [0.62 – 2.33]	1.48 [0.47 – 4.72]	
Acute reperfusion treatment								0.12
No	251 (57.4%)	151 (34.6%)	35 (8.0%)		Referent	1.32 [0.88 – 1.98]	2.09 [1.03 – 4.22]	
Yes	80 (43.0%)	68 (36.6%)	38 (20.4%)		Referent	1.02 [0.43 – 2.43]	1.85 [0.72 – 4.85]	
Occlusion site								0.07
ICA	121 (58.7%)	62 (30.1%)	23 (11.2%)		Referent	1.76 [0.95 – 3.28]	2.88 [1.03 – 8.37]	
MCA	210 (50.4%)	157 (37.6%)	50 (12.0%)		Referent	1.05 [0.70 – 1.59]	1.82 [0.99 – 3.35]	
Perfusion study								0.40
No	149 (48.9%)	110 (36.1%)	46 (15.1%)		Referent	1.00 [0.61 – 1.60]	1.29 [0.65 – 2.60]	
Yes	182 (57.2%)	109 (34.3%)	27 (8.5%)		Referent	1.33 [0.80 – 2.20]	3.00 [1.30 – 7.10]	

Odds ratio [95% CI]

Figure 3. Subgroup analysis of infarct progression according to leptomeningeal collateral circulation status.
ICA indicates internal carotid artery; LMC, leptomeningeal collateral; and MCA, middle cerebral artery.

blunted normal physiologic response of cerebral vessels in hyperglycemic conditions.[28] Hyperglycemia is known to be associated with impaired nitric oxide–mediated vasodilatation, which results in the impairment of collateral flow recruitment.[28] The production of nitric oxide increases ≈20-fold during the first few minutes after LVO, and nitric oxide–mediated vasodilatation is one of the major contributors of LMC recruitment.[29] A failure of this physiological response may exacerbate the ischemic damage to neural tissue by impairing the cerebral autoregulation.[27] The association between diabetes and poor LMC grade from our study may support the result of a recent report that identified poor functional outcomes after thrombectomy in patients with poor prestroke glycemic control.[30] Additionally, the mitigating influence of the LMC extent on infarct progression in patients with diabetes and hypertension in our subgroup analyses may imply that a good LMC extent does not guarantee a sufficient LMC flow even in patients with mild LVO when accompanied by vascular comorbidities. Since hyperglycemia is also associated with poor functional outcomes after endovascular treatment in patients with a good LMC, further exploration is warranted to determine the optimal range of the blood

glucose–level targets according to the LMC extent in patients with mild LVO.[31]

Another important finding of our study is that a poor LMC extent was associated with more prominent neurological symptom progression when END had occurred. Although rescue endovascular therapy in patients with minor stroke has been shown to be effective and safe in previous studies, the functional outcome of patients who experienced END was worse than that of patients without clinical deterioration.[16,32] Therefore, in addition to the need for a randomized trial that evaluates up-front endovascular treatment in patients with mild LVO, there is also an urgent need to establish a strategy to prevent infarct progression and END in patients with mild LVO. The ongoing clinical trials that are evaluating the potential benefits of ischemic preconditioning (REMOTE-CAT [REMOTE Ischemic Perconditioning Among Acute Ischemic Stroke Patients; NCT03375762], TRICS-9 [Clinical Trial on Remote Ischemic Conditioning In Acute Ischemic Stroke Within 9 Hours of Onset in Patients Ineligible to Rcanalization Therapies; NCT04400981]) might provide additional treatment options for preventing imaging and clinical deterioration in patients with mild

LVO.[33] Based on the association between a poor LMC and neurological worsening that was identified in the current study, augmenting the collateral flow through therapeutic-induced hypertension may be another option that warrants future research in this population.[34]

ASPECTS is a well-established method for estimating early ischemic changes on noncontrast CT image and has provided the criteria for selecting patients for reperfusion treatment in previous randomized trials.[35] ASPECTS scoring system is also applicable to DWI–magnetic resonance imaging, and DWI-ASPECTS is known to correlate with initial stroke severity and predict patient outcomes after thrombectomy with better inter-rater agreement compared with CT-ASPECTS.[36–38] However, certain discrepancies exist between CT- and DWI-ASPECTS due to differences in image acquisition technique, image axis, and rating scheme, and DWI-ASPECTS is reported to be ≈1 point lower than CT-ASPECTS.[36] The REVASCAT (Randomized Trial of Revascularization With Solitaire FR Device Versus Best Medical Therapy in the Treatment of Acute Stroke Due to Anterior Circulation Large Vessel Occlusion Presenting Within 8 Hours of Symptom Onset) trial considered the difference between CT- and DWI-ASPECTS and applied different exclusion criteria on the basis of imaging modalities (excluded patients with CT-ASPECTS <7 points and those with DWI-ASPECTS <6 points).[4] On the other hand, a recent secondary analysis of the DAWN (Clinical Mismatch in the Triage of Wake Up and Late Presenting Strokes Undergoing Neurointervention With Trevo) study did not report a significant confounding effect of different imaging modalities when examining serial ASPECTS change at baseline and at 24 hours.[39] In our study, approximately half of the patients had different baseline and follow-up imaging modalities. Considering this discrepancy, we rated the DWI-ASPECTS as positive when the affected lesions exceeded one-third of the ASPECTS template. The poor LMC extent tended to be related with infarct progression, despite inconsistent imaging modalities between baseline and follow-up ASPECTS. After validation in a larger cohort, the rating scheme of DWI-ASPECTS used in our study can provide pragmatic guidance for overcoming the inevitable gap between baseline and follow-up imaging modalities in real-world data.

This study has several limitations. First, although we obtained the clinical data from a multicenter, nationwide prospectively collected stroke registry, the image acquisition protocols at each center were not standardized. Thus, in our cohort, there may be discrepancies in baseline and follow-up brain imaging. However, poor LMCs were consistently associated with infarct lesion progression, additionally adjusted for differences in baseline and follow-up imaging modalities, and when tested in a subset with identical baseline and follow-up imaging modalities (Table S2 and Supplemental Data). Second, unmeasured confounders might affect the infarct progression, including angiographic characteristics of occlusion site, asymptomatic intracranial steno-occlusion, blood pressure management after admission, and medication adjustments when patients develop END. Third, collateral flow was assessed by images obtained from diverse imaging modalities in this study. The measurements of the LMC grade using time-of-flight magnetic resonance angiography may be heterogeneous with the measurements obtained from the other vascular neuroimaging. Fourth, this study did not evaluate advanced neuroimaging information, including CT perfusion or magnetic resonance perfusion images. Finally, this study mainly evaluated Asian patients, and care must be taken for extrapolating the results of this study because there may be differences in the stroke causes, the prevalence of vascular risk factors, or genetic characteristics, depending on ethnicity, in different populations.

CONCLUSIONS

Our study showed that infarct progression might develop in patients with poor LMC, even in patients with acute mild LVO who were supposed to have tenacious collateral flow. Baseline LMC score need to be considered when assessing risk of infarct progression, and it might help in selecting suitable candidates for advanced treatment including up-front EVT in patients with stroke with LVO and who have mild symptoms.

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Supplemental Materials

Supplemental Material

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