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Rescue therapy of early neurological deterioration in lacunar stroke

Soo-Hyun Park[1], Jonguk Kim[2], Cindy W. Yoon[2], Hee-Kwon Park[2*] and Joung-Ho Rha[2]

Abstract

Background Early neurological deterioration (END) occurs in many patients with acute ischemic stroke due to a variety of causes. Although pharmacologically induced hypertension (PIH) and anticoagulants have been investigated in several clinical trials for the treatment of END, the efficacy and safety of these treatments remain unclear. Here, we investigated whether PIH or anticoagulation is better as a rescue therapy for the progression of END in patients with lacunar stroke.

Methods This study included patients with lacunar stroke who received rescue therapy with END within 3 days of symptom onset between April 2014 and August 2021. In the PIH group, phenylephrine was administered intravenously for 24 h and slowly tapered when symptoms improved or after 5 days of PIH. In the anticoagulation group, argatroban was administered continuously intravenously for 2 days and twice daily for next 5 days. We compared END recovery, defined as improvement in NIHSS from baseline, excellent outcomes (0 or 1 mRS at 3 months), and safety profile.

Results Among the 4818 patients with the lacunar stroke, END occurred in 147 patients. Seventy-nine patients with END received PIH (46.9%) and 68 patients (46.3%) received anticoagulation therapy. There was no significant difference in age ($P=0.82$) and sex ($P=0.87$) between the two groups. Compared to the anticoagulation group, the PIH group had a higher incidence of END recovery (77.2% vs. 51.5%, $P<0.01$) and excellent outcomes (34.2% vs. 16.2%, $P=0.04$). PIH was associated with END (HR 2.49; 95% CI 1.06–5.81, $P=0.04$). PIH remained associated with END recovery (adjusted HR 3.91; 95% CI 1.19–12.90, $P=0.02$). Safety outcomes, like hemorrhagic conversion and mortality, were not significantly different between the two groups.

Conclusions As a rescue therapy for the progression of END in lacunar stroke patients, PIH with phenylephrine was more effective with similar safety compared to anticoagulation with argatroban.

Keywords Early neurological deterioration, Rescue therapy, Pharmacologically induced hypertension, Anticoagulation, Lacunar stroke, Branch atheroma

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Introduction

Early neurological deterioration (END) often occurs in patients with acute ischemic stroke [1–3] and is linked to a poor prognosis [4]. Therefore, when END occurs, many stroke physicians attempt various treatments to mitigate it [5]. A primary cause of END among several mechanisms is cerebral hypoperfusion [6, 7]. In this case, physicians aim to increase cerebral perfusion by augmenting cerebral blood flow (CBF).

For treating END, colloids and crystalloids, which are volume expanders, are utilized to boost intravascular blood volume. More patients showed an improvement in their NIH stroke scale (NIHSS) score after END when administered low doses of colloids compared to crystalloids [3, 8]. However, using colloids at high doses or for prolonged durations can lead to acute kidney injury (AKI), and colloids are inappropriate for acute ischemic stroke patients with kidney disease [9–11].

Alternative treatments for END include pharmacologically induced hypertension (PIH) and anticoagulation. The efficacy of PIH in promoting END recovery and improving functional outcomes has been demonstrated [8, 12, 13]. While anticoagulation using low molecular weight heparins or heparinoids is not recommended for acute ischemic stroke [14], argatroban has been approved as a therapeutic option to improve END recovery in acute ischemic stroke in Japan and Korea [15–18]. However, previous studies have not clarified whether PIH or argatroban is effective and safe for treating stroke progression-related END in lacunar stroke patients. This study aims to determine which treatment is more beneficial as rescue therapy for lacunar stroke patients who experience END.

Methods

Study population

This retrospective study was based on a prospective single-center stroke registry from Inha University Hospital. We screened individuals over 19 years old who were admitted between April 2014 and August 2021 and diagnosed with acute ischemic stroke within 7 days of symptom onset. We selected lacunar stroke patients (both small vessel occlusion and branch atheroma) with END who showed no symptom improvement after normal saline loading (about 300 to 500 mL) for analysis (Fig. 1). A diagnosis of lacunar stroke was made if the patient had typical clinical lacunar syndromes [19], had a neurological deficit lasting over 24 h, showed no evidence of

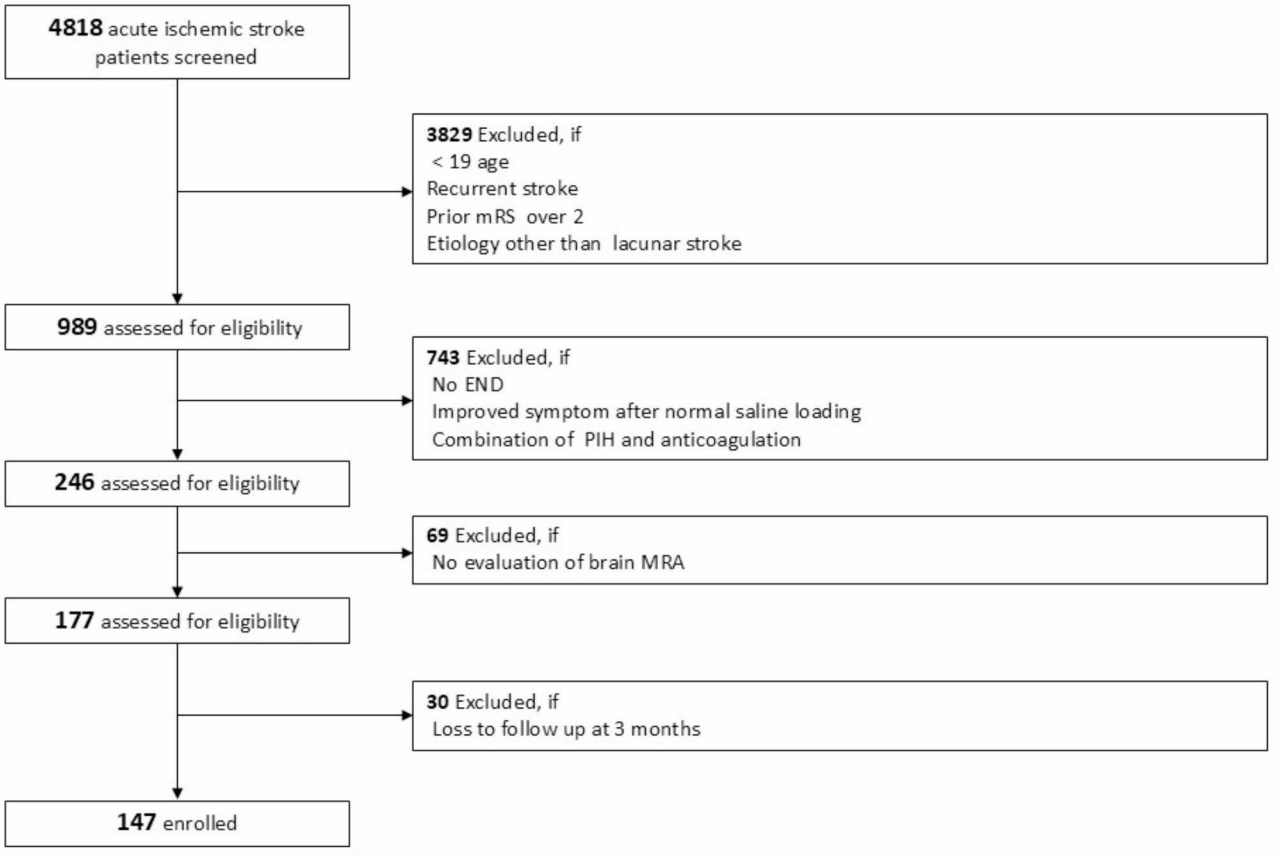

Fig. 1 Study flow. mRS, modified Rankin Scale; END, early neurological deterioration; PIH, pharmacologically induced hypertension; brain MRA; brain magnetic resonance angiography

cerebral cortical dysfunction, and had computed tomography (CT)/magnetic resonance image (MRI) indicating a focal infarction in the distribution of perforator vessels with a diameter≤20 mm [20]. END was defined as an increase of 2 or more in the total NIHSS score or an increase of 1 or more in the motor NIHSS score within the initial 72 h of admission [21, 22].

The following exclusion criteria were applied: (1) age less than 19 years (n=126), (2) END related to stroke recurrence (n=479), (3) previous modified Rankin Scale (mRS) score greater than 2 (n=364), (4) etiology other than lacunar stroke (n=3401), (5) presence of other major neurological diseases such as brain tumor, seizure, infectious disease, etc. (n=214), (6) improvement of END after normal saline loading (n=45), (7) concomitant use of phenylephrine and argatroban (n=7), (8) lack of brain magnetic resonance angiography (MRA) assessment (n=69), and (9) lack of information on mRS at 3 months after acute ischemic stroke (n=30).

Baseline characteristics and image findings

Baseline characteristics of patients, including risk factors and laboratory results, were reviewed using electronic medical records. Neurological assessments were conducted using the NIHSS and mRS. The NIHSS scores were assessed by specialized nurses or neurointensivists every 8 h for 7 days, according to the stroke center policy in Korea. MRI and MRA diagnostics were conducted using a 3T whole-body scanner. The location of infarction was categorized as thalamus, corona radiata, internal capsule, basal ganglia, and pons. The severity of cerebral white matter intensity was evaluated based on the Fazekas criteria, using fluid-attenuated inversion recovery and T2 sequences (T2 FLAIR). The number of microbleeds was determined using gradient echo sequences (GRE) [23]. When END occurred, brain CT or MRI was reassessed within 24 h from the END event.

Procedures

When END occurred, clinicians first administered a normal saline loading (approximately 300 to 500 ml) to expand the intracranial volume. If END did not improve after the normal saline loading, physicians determined a rescue treatment to improve END. The decision between PIH and anticoagulation was based on the physician's discretion (Fig. 2).

In cases of PIH, phenylephrine (0.12 mg/mL) was administered. As a selective α1-agonist, phenylephrine increases blood pressure by peripheral vasoconstriction without direct cerebral vasoconstriction, because of the low α1-receptors in cerebral vessels [24, 25]. The method for administering phenylephrine was according to recommendations from a previous study [12, 13]. Phenylephrine was slowly tapered (10 mL/h) after 24 h if neurological stabilization was observed in the responders or after 5 days of use. If clinical deterioration occurred again during this tapering period, PIH was restarted to raise the systolic blood pressure (SBP) for neurological improvement. The maximum systolic blood pressure of patients treated for PIH was 180 mmHg, and the goal was to increase blood pressure by 15–25% from baseline [12, 13].

In cases where anticoagulation is required, argatroban has been selected. As a selective thrombin inhibitor, argatroban has recently gained attention for its ability to increase blood flow effectively. Argatroban was administered according to recommendations from previous studies: for the first 2 days, 60 mg was diluted with intravenous (IV) fluid and infused continuously over 24 h. For the next 5 days, 10 mg was diluted with IV fluid and injected twice daily (morning and evening) over 3 h each time [14, 16, 26, 27].

For safety considerations, phenylephrine was immediately discontinued if patients developed symptoms. Argatroban infusion was also discontinued if it was interrupted for ≥4 consecutive hours or if intracranial or major bleeding occurred.

Outcomes

The primary outcome was the proportion of END recovery, defined as a decrease in NIHSS by more than 2 points or improved motor symptoms within the first 7

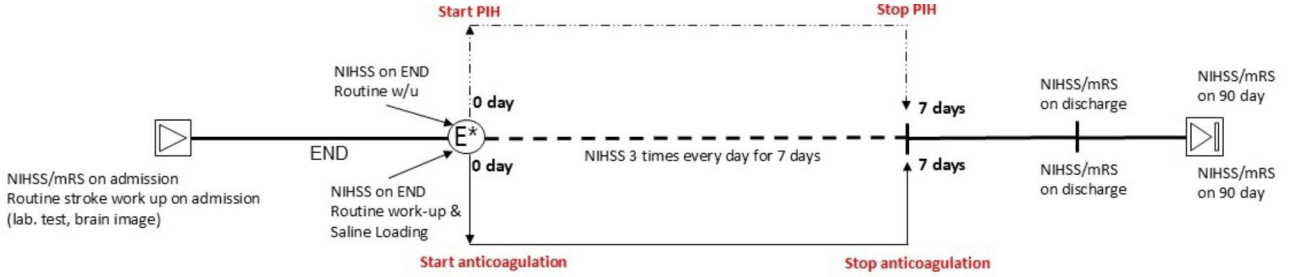

Fig. 2 Schematic overview of the protocol. E*, enrollment; END, early neurological deterioration; PIH, pharmacologically induced hypertension; NIHSS, National Institutes of Health Stroke Scale; mRS, modified Rankin Scale. E*, * If the patient's symptoms did not improve despite normal saline loading, the treatment option was determined by the physician's preference. END, neurological deterioration within 2 days after symptom onset

days when using either phenylephrine or argatroban. The secondary outcome was the proportion of excellent functional outcomes (mRS 0 to 1) at 3 months from the onset of acute ischemic stroke.

Additionally, we assessed safety outcomes, including stroke recurrence, hemorrhagic complications, coronary events, all-cause death, and various side effects from the use of phenylephrine or argatroban. Hemorrhagic complications included events such as hemorrhagic stroke, gastrointestinal bleeding, craniotomy for hematoma removal, administration of tranexamic acid, and transfusion of ≥1 unit of blood.

Statistical methods

Mean (±standard deviation) or median (interquartile range, [IQR]) was calculated for continuous variables and compared using either a Student's *t*-test or a Mann–Whitney *U* test. Categorical variables were presented as frequencies (percentages) and compared using the χ^2 test or Fisher's exact test. Logistic regression analysis was applied to identify potential factors associated with END recovery. Covariates with statistically significant differences ($P<0.1$) from univariate analysis and those with clinical importance were adjusted for multivariate analysis.

Propensity score matching (PSM) analysis was executed to reduce selection bias in this study. To estimate PSM, a patient in the phenylephrine group was matched with a patient in the argatroban group using the nearest neighbor rule within a caliper width of 0.1 of the standard deviation of the propensity score [28]. In the matched populations, continuous variables were compared between the argatroban and phenylephrine groups using a Student's *t*-test, whereas categorical variables were compared with the Fisher exact test or the χ^2 test.

All tests of significance were 2-tailed, and $P<0.05$ was considered significant. All statistical analyses were performed using SPSS Statistics version 26.0 (SPSS Inc., Chicago, IL, USA).

Table 1 Baseline characteristics of the study population

Characteristics	Treatment		
	Phenylephrine (*n* = 79, 53.7%)	Argatroban (*n* = 68, 46.3%)	*P* value
Age†, years	64.4 ± 11.5	64.8 ± 11.1	0.82
Sex (man)¶	46 (58.2)	38 (55.9)	0.87
Diabetes mellitus¶	35 (44.3)	20 (29.4)	0.09
Hypertension¶	54 (68.4)	42 (61.8)	0.49
Dyslipidemia¶	18 (22.8)	29 (42.6)	0.01
History of smoking¶	28 (35.4)	22 (32.4)	0.73
History of prior stroke¶	7 (8.9)	8 (11.8)	0.60
Intravenous thrombolysis¶	8 (10.1)	5 (7.4)	0.77
Body mass index†, Kg/m^2	24.8 ± 3.6	24.6 ± 3.0	0.72
Laboratory results			
Total cholesterol†, mg/dL	186.46 ± 42.85	185.68 ± 48.23	0.92
HbA1C†, %	6.7 ± 1.7	6.6 ± 1.9	0.78
C-reactive protein†, mg/dL	0.36 ± 0.89	0.61 ± 2.29	0.40
Branch atheroma¶	24 (30.4)	38 (55.9)	< 0.01
Existence of cerebral Microbleeds¶	12 (15.6)	14 (20.6)	0.52
Fazekas scale (2 or more) ¶	18 (22.8)	20 (29.4)	0.45
SBP on admission†, mmHg	157.4 ± 29.3	167.1 ± 27.3	0.19
DBP on admission†, mmHg	90.9 ± 17.8	97.8 ± 18.3	0.14
SBP on END†, mmHg	137.0 ± 21.9	157.1 ± 20.0	< 0.01
DBP on END†, mmHg	77.8 ± 13.2	88.9 ± 16.0	< 0.01

Data are presented as mean ± standard deviation†, or number (%) ¶

END, early neurological deterioration; SBP, systolic blood pressure; DBP, diastolic blood pressure

Results

A total of 4818 acute ischemic stroke patients were screened. Figure 1 illustrates the selection process. Of these, 4671 patients were excluded, resulting in 147 patients being recruited for the study. Among these, 79 patients received PIH treatment, and 68 received argatroban treatment.

The baseline characteristics are presented in Table 1. Rescue therapy was administered irrespective of the presence of microbleeds or cerebral white matter hyperintensities. The two groups showed no significant difference in age (64.4 years for PIH vs. 64.8 years for argatroban, $P=0.82$) and sex (58.2% male in the PIH vs. 55.9% male in the argatroban, $P=0.87$). However, there were significant differences between the two groups in dyslipidemia (22.8%, in the PIH vs. 42.6% in the argatroban; $P=0.01$) and branch atheroma presence (30.4% in the PIH vs. 55.9% in the argatroban; $P<0.01$). When END occurred, the PIH group had lower SBP (137 mmHg vs. 157 mmHg) and DBP (77.8 mmHg vs. 88.9 mmHg) compared to the argatroban group ($P<0.01$). Most other characteristics showed no statistically significant difference.

After PSM, 48 patients who received phenylephrine were matched to 48 patients who received argatroban. A significant difference in branch atheroma remained between the two groups (Supplementary file 1). SBP over 145mmHg was more prevalent in the argatroban group (74.5%) than in the PIH group (34.0%; $P<0.01$).

The two groups showed no difference in NIHSS score on admission ($P=0.61$), as presented in Table 2. END recovery was noted in 77.2% of the PIH group and 51.5% of the argatroban group ($P<0.01$). A more favorable trend in NIHSS score distribution was observed in the PIH group at discharge (median 4 vs. 5; $P<0.01$, Fig. 3). Regarding mRS at 3 months, the PIH group showed better functional outcomes, with 34.2% achieving mRS 0–1, compared to 16.2% in the argatroban group ($P=0.04$).

Table 2 Treatment efficacy and safety outcome of the study population

Characteristics	Treatment		
	Phenylephrine (*n* = 79, 53.7%)	Argatroban (*n* = 68, 46.3%)	*P* value
Treatment efficacy			
END recovery[¶]	61 (77.2)	35 (51.5)	< 0.01
NIHSS on admission[§*]	5 (3–6)	5 (2–7)	0.61
NIHSS on END[§*]	7 (5–9)	8 (6–10)	< 0.01
NIHSS on discharge[§*]	4 (1–6)	5 (4–8)	< 0.01
Excellent outcome (mRS 0–1) at 3 months[§*]	27 (34.2)	11 (16.2)	0.04
Safety outcome			
Stroke recurrence[†], n (%)	1 (1.5)	2 (2.9)	0.54
Hemorrhagic complication[£], n (%)	0 (0)	1 (1.6)	0.46
Coronary events[¥], n (%)	0 (0)	0 (0)	N/A
All-cause death[¥], n (%)	1 (1.5)	0 (0)	0.93
Other side effect[¥], n (%)	2 (2.5)	1 (1.6)	0.54

Data are presented as mean ± standard deviation[†], median (interquartile range, IQR) [§], or number (%)[¶]

*The Mann-Whitney U test was used

[£]during 3 months; [¥] during admission

N/A, not applicable

NIHSS, National Institutes of Health Stroke Scale; END, early neurological deterioration

There was no significant difference between the two groups in major safety outcomes, both at admission and during the 3 months follow-up period. Three patients experienced a stroke recurrence over the 3 months follow-up (1.5% in the PIH vs. 2.9% in the argatroban, $P=0.54$). In the PIH group, no patient had major hemorrhagic complications during admission. However, one patient in the argatroban group experienced symptomatic intracranial hemorrhage ($P=0.46$). One patient in the PIH group died of pneumonia-related respiratory failure, which was unrelated to phenylephrine. Three patients reported other side effects (palpitation in 1, dyspnea in 1, urticaria in 1) related to rescue therapy. No coronary events were reported in either group.

Table 3 Multivariate logistic regression analysis of the factors related to END recovery

Value	Unadjusted odds ratio (95% CI)	*P* value	Adjusted odds ratio (95% CI)	*P* value
Age < 65 years	2.81 (1.38–5.75)	< 0.01	2.29 (1.03–5.10)	0.04
Sex, man	0.60 (0.30–1.21)	0.15	0.76 (0.35–1.68)	0.50
Dyslipidemia	1.44 (0.70–2.96)	0.32	0.93 (0.40–2.19)	0.88
Branch atheroma	1.96 (0.98–3.91)	0.06	0.69 (0.31–1.54)	0.37
Phenylephrine (versus argatroban)	3.20 (1.57–6.49)	0.01	2.49 (1.06–5.81)	0.04
NIHSS on END ≥ 8	0.46 (0.23–0.93)	0.03	0.67 (0.30–1.50)	0.33
SBP on END > 145 mmHg	0.36 (0.18–0.75)	< 0.01	0.60 (0.26–1.37)	0.23

Adjusted covariates were age, sex, dyslipidemia, branch atheroma, phenylephrine, NIHSS on END (≥ 8), and SBP on END (> 145 mmHg)

NIHSS, National Institutes of Health Stroke Scale; END, early neurological deterioration; SBP, systolic blood pressure

The unadjusted hazard ratio (HR) for END recovery was 2.81 (95% CI 0.17–0.73, $P<0.01$) for those under 65

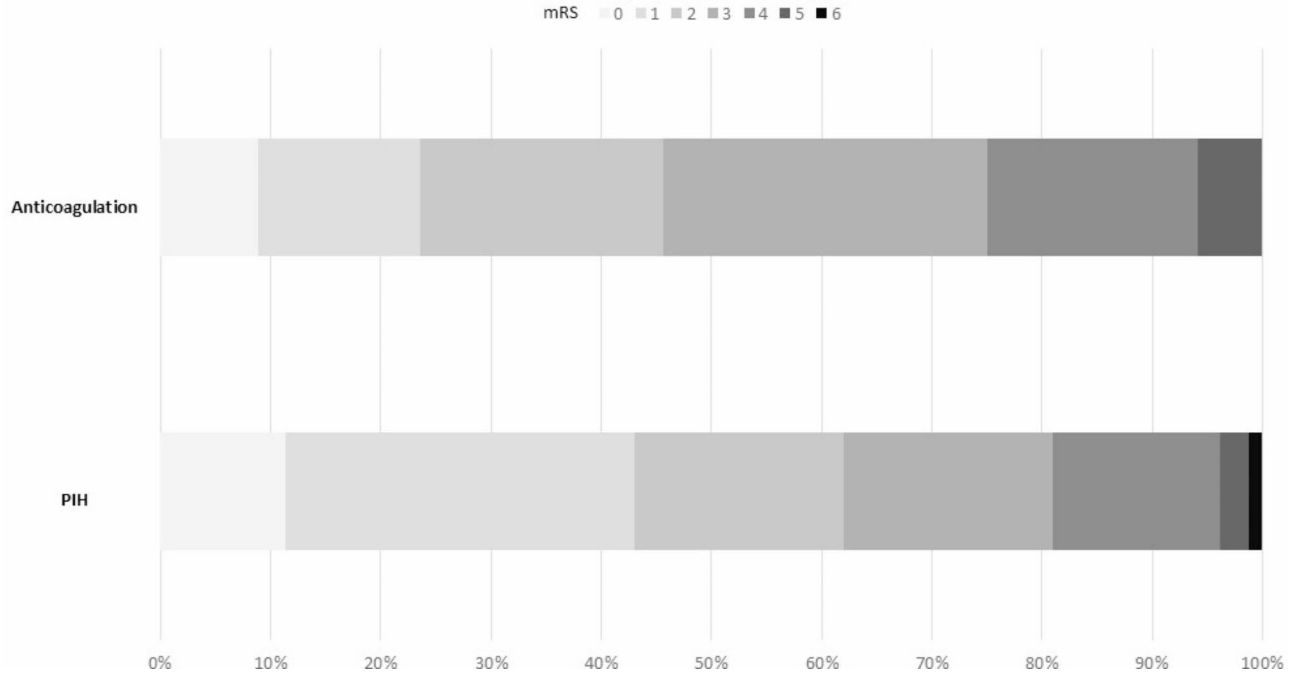

Fig. 3 Functional outcomes at 3 months. PIH, pharmacologically induced hypertension; mRS, modified Rankin Scale

years and 3.12 (95% CI 1.57–6.49, $P=0.01$) for PIH treatment (Table 3). Additionally, HRs for other factors associated with END recovery were 0.46 for an NIHSS over 8 at END (95% CI 0.23–0.93, $P=0.03$) and 0.36 for a SBP > 145 mmHg at END (95% CI 0.23–0.93, $P=0.03$). After adjustment for age, sex, dyslipidemia, branch atheroma, use of phenylephrine, NIHSS score on END (≥8), and SBP on END (>145 mmHg), both PIH (HR 2.49; 95% CI 1.06–5.81, $P=0.04$) and being under 65 years (HR 2.29; 95% CI 1.03–5.10, $P=0.04$) were associated with END recovery. Branch atheroma was not a significant factor affecting END recovery (unadjusted HR 1.96; 95% CI 0.98–3.91, $P=0.06$, adjusted HR 0.69; 95% CI 0.31–1.54, $P=0.37$).

Further, when categorizing patients by small vessel occlusion and branch atheroma, the impact of PIH and argatroban on END recovery was evident (Additional file 2). PIH was more effective in promoting END recovery than argatroban for both small vessel occlusion (80.0% vs. 60.0%, $P=0.05$) and branch atheroma (75.0% vs. 44.7%, $P=0.02$).

The comparison of END recovery between propensity-matched patients who received PIH and those who received agatroban is presented in Table 4. Univariate analysis demonstrated that PIH was significantly associated with END recovery (HR 3.37; 95% CI 1.34–8.48, $P=0.01$). This association persisted in multivariable analysis (selective variables, HR 3.91; 95% CI 1.19–12.90, $P=0.02$; all covariates, OR 7.30, 95% CI 1.56–34.19, $P=0.01$).

Discussion

We investigated the efficacy and safety of PIH versus argatroban in the treatment of END in lacunar stroke. Our findings showed that PIH appears to be a safe and superior rescue treatment for END, enhancing functional independence at 3 months compared to argatroban.

Table 4 Univariable and multivariable analysis association between treatments and END recovery among propensity-matched patients

Model	Odd ratio (OR, 95% CI)	*P* value
Univariable for propensity		0.01
Phenylephrine	3.37 (1.34–8.48)	
Argatroban	0.30 (0.12–0.75)	
Multivariable for propensity and selective variables†		0.02
Phenylephrine	3.91 (1.19–12.90)	
Argatroban	0.26 (0.08–0.84)	
Multivariable for propensity and all covariates¶		0.01
Phenylephrine	7.30 (1.56–34.19)	
Argatroban	0.14 (0.03–0.64)	

† Selective variables included age, man, dyslipidemia, branch atheroma, NIHSS on END (≥8), and SBP on END (>145 mmHg)

¶ For a list of covariates, see supplementary 1

Shutdown of collateral circulation is associated with the growth of the infarct core, leading to the occurrence of END [29]. There is a relationship between arterial blood pressure and collateral circulation of intracranial vessels [30–32]. When cerebral autoregulation is impaired in ischemic lesions due to stroke, cerebral blood flow becomes increasingly dependent on arterial pressure [33]. Elevated blood pressure, especially when SBP > 170 mmHg, is associated with improved development of collateral circulation [32].

The sympathetic nerve fibers that wrap around cerebral arteries play a role in improving CBF by increasing cerebrovascular tone [34, 35]. The outflow of cerebral noradrenaline into the internal jugular vein influences tonic sympathetic activity towards the cerebral vasculature [34]. This mechanism supports the role of α-adrenergic modulation in the cerebral vasculature in the treatment of END.

Phenylephrine, a sympathomimetic drug, more effectively and directly prevents a decrease in CBF than argatroban by elevating blood pressure, either through an increase in cardiac output and/or total peripheral resistance [34]. Therefore, the difference in efficacy can be attributed to the cerebrovascular structure and mechanisms involved. PIH might enhance collateral circulation by elevating cerebral perfusion pressure [13, 34, 36].

Argatroban directly inhibits platelet aggregation and endothelin-1 release during thrombin clotting [14]. It may constrain microthrombi formation by inhibiting thrombin due to ischemia, protecting neuronal cells, and limiting neurological deficits [14, 37]. It can also increase cerebral blood flow and reduce infarct size, particularly in the penumbral area.

Our results showed that both phenylephrine and argatroban appear to be beneficial in improving END in lacunar stroke. Interestingly, phenylephrine seems to offer better recovery from END than argatroban, due to the different therapeutic effects mentioned above. In the phenylephrine group, 77.2% of patients experienced END recovery compared to 51.5% in the argatroban group ($P<0.01$). A higher proportion of patients treated with phenylephrine had an excellent outcome (mRS 0–1) at 3 months compared to those treated with argatroban (34.2% vs. 16.2%, $P=0.04$). After adjusting for covariates through propensity matching, phenylephrine remained a more effective treatment for END recovery than argatroban.

We further evaluated the effect of rescue therapy on END recovery by stratifying subjects into small vessel occlusion (SVO) and branch atheroma. In our study, branch atheroma was identified in nearly one-third of cases, while the remaining two-thirds were classified

as small vessel occlusion. The use of phenylephrine for improving END demonstrated efficacy in 80% of small vessel occlusion cases (compared to 60% with argatroban, $P=0.05$) and in 75% of branch atheroma cases (compared to 44.7% with argatroban, $P=0.02$). This suggests that phenylephrine is superior to argatroban in treating both branch atheroma and small vessel occlusion.

The benefits of PIH and anticoagulant therapy for acute ischemic stroke patients remain controversial in previous studies [13, 38–40]. To date, there have been no studies directly comparing the safety and efficacy of these two treatments [13–16, 41–46]. Additionally, regarding END treatment for lacunar stroke, published guidelines do not offer a definitive recommendation [38]. However, our study suggests that both PIH and argatroban treatments are safe and effective for patients with END. Especially, phenylephrine is more effective than argatroban in treating both branch atheroma and small vessel occlusion.

PIH and argatroban did not result in a significant increase in serious adverse events. This finding is consistent with previous studies that reported only a nonsignificant increase in hemorrhagic stroke and arrhythmias in patients treated with PIH or argatroban [12–14, 24, 46, 47]. These treatments do not result in clinically relevant increases in intracranial pressure [48]. Although PIH increased cerebral perfusion pressure more in the damaged hemisphere, it did not cause a significant increase in intracranial pressure during intracranial monitoring [12, 13]. These results indicate that the risk of intracranial hemorrhage is low in patients receiving PIH. Argatroban does not induce or potentiate heparin-induced thrombocytopenia, causes less bleeding than heparin for the same anticoagulant effect, and is well tolerated in various settings [14]. Due to its rapid onset of action, low bleeding tendency, and lack of immunogenicity, argatroban has demonstrated both efficacy and safety in acute ischemic stroke [14]. These findings suggest that PIH and argatroban therapy are theoretically and clinically associated with a low risk of intracranial hemorrhage. Additionally, our study confirmed that physicians should consider SBP and potential related side effects, such as intracranial hemorrhage, when making treatment decisions for patients with END. In cases with initially elevated SBP, argatroban treatment was preferred. In contrast, PIH was preferred in cases with low SBP.

Our study has several limitations. Our study was a single-center, retrospective study with a relatively small sample size. Although we performed multivariable analysis or PSM, further studies involving large and more diverse populations are needed to generalize our findings. There is potential selection bias because physicians may choose treatments for END based on their clinical experience and preferences. Consequently, the dosages and timing of administration of argatroban and phenylephrine were adjusted based on patient conditions. The dosages of argatroban and the optimal SBP target followed recommendations from previous studies without additional validation in this study. Further studies with larger cohorts are needed to establish specific protocols based on patient characteristics. We did not evaluate the mechanisms related to PIH or argatroban. We plan to analyze changes in serial MRI, including brain perfusion imaging, in future studies. Our study subjects were lacunar stroke patients in Korea. Genetic or environmental factors, as well as other etiologies, may influence systemic and cerebral hemodynamics in response to treatments. We excluded patients with improved END after normal saline loading. Further studies are warranted to investigate the effect of systemic and cerebral hemodynamics, including treatments and normal saline loading, on END.

Conclusions

Our study suggests that both therapeutic-induced hypertension and argatroban are safe and feasible for treating END in lacunar stroke. Notably, therapeutic-induced hypertension treatment demonstrated more promising results in enhanced END recovery and excellent functional outcomes at 3 months compared to the anticoagulation treatment.

Abbreviations

AKI	Acute Kidney Injury
CBF	Cerebral Blood Flow
CT	Computed Tomography
END	Early Neurological Deterioration
FLAIR	Fluid-Attenuated Inversion Recovery
GRE	Gradient Echo Sequences
HR	Hazard Ratio
IQR	Interquartile Range
MRA	Magnetic Resonance Angiograph
MRI	Magnetic Resonance Image
mRS	modified Rankin Scale
NIHSS	NIH Stroke Scale
PIH	Pharmacologically Induced Hypertension
PSM	Propensity Score Matching

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12883-024-03825-7.

Supplementary Material 1

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Not applicable.

Author contributions

SHP and HKP: study concept and design, acquisition of data, analysis and interpretation of data, drafting of the manuscript, and revision of the manuscript; SHP, JWK and HKP: critical revision of the manuscript for important intellectual content; CWY and JHR: acquisition of data, analysis and interpretation of data; SHP, JWK and HKP: statistical analysis; SHP, JWK, CWY, HKP, and JHR: technical or material support; HKP: obtainment of funding, revision of the manuscript and study supervision.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
The study protocol was approved by the institutional review board of Inha University Hospital, Incheon, Korea (IRB number: 2019-06-024).

Competing interests
The authors declare no competing interests.

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