Stroke: Vascular and Interventional Neurology

ORIGINAL RESEARCH

Association Between Estimated Pulse Wave Velocity and Endovascular Thrombectomy Outcome: A Secondary Analysis of the OPTIMAL-BP Trial

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BACKGROUND: The link between arterial stiffness, measured by estimated pulse wave velocity (ePWV), and outcomes following endovascular thrombectomy (EVT) has not been tested. This study aimed to determine whether ePWV predicts post-EVT outcome in patients with acute ischemic stroke.

METHODS: This was a secondary analysis of the OPTIMAL-BP (Outcome in Patients Treated With Intraarterial Thrombectomy–Optimal Blood Pressure Control) trial, which enrolled 302 EVT patients from 19 stroke centers in South Korea between June 18, 2020 and November 28, 2022. The ePWV was calculated using a regression equation based on age and mean blood pressure (BP) at trial enrollment: $ePWV = 9.587 - 0.402 \times age + 4.560 \times 10^{-3} \times age^2 - 2.621 \times 10^{-5} \times age^2 \times mean\ BP + 3.176 \times 10^{-3} \times age \times mean\ BP - 1.832 \times 10^{-2} \times mean\ BP$. The primary outcome was functional independence at 3 months, defined as a modified Rankin Scale score of 0–2. Logistic, ordinal, or linear regression analyses were employed to estimate adjusted odds ratios with 95% CIs for outcomes per 1 m/s or quartile ePWV increase.

RESULTS: Among 302 patients (mean age 73.1±11.5 years, 59.6% men), higher ePWV was independently associated with a lower likelihood of functional independence at 3 months (adjusted odds ratio, 0.80 [95% CI, 0.68–0.94] per 1 m/s increase; adjusted odds ratio, 0.36 [95% CI, 0.14–0.95] for the fourth quartile). A reduction in ePWV at 24 hours after EVT increased the likelihood of functional independence at 3 months in patients receiving conventional BP management (adjusted odds ratio, 3.41 [95% CI, 1.02–11.38]) but not in those receiving intensive BP management. Incorporating ePWV significantly improved

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prognostic model performance, with net reclassification improvement of 0.28 (95% CI, 0.06–0.50) and integrated discrimination improvement of 0.02 (95% CI, 0.003–0.04).

CONCLUSION: The ePWV independently predicts functional independence after EVT, suggesting its potential as a practical prognostic indicator using age and baseline BP.

Key Words: arterial stiffness ■ endovascular thrombectomy ■ estimated pulse wave velocity ■ ischemic stroke ■ outcome

Endovascular thrombectomy (EVT) has revolutionized the management of acute ischemic stroke due to large cerebral artery occlusion. Despite its effectiveness in reperfusion and improving functional outcomes, many patients remain functionally dependent and experience poor quality of life after EVT.[1] Recent randomized controlled trials and metaanalyses indicate that conventional blood pressure (BP) management leads to better functional outcomes than intensive BP management without increasing symptomatic intracerebral hemorrhage.[2–4] Because BP is a major determinant of arterial stiffness and arterial stiffness is closely related with BP,[5] the impact of arterial stiffness on post-EVT outcome requires further investigation.

Carotid-femoral pulse wave velocity (PWV) is the gold standard for measuring arterial stiffness.[6] The carotid-femoral PWV enhances cardiovascular risk prediction and is recommended by the 2023 European Society of Hypertension guidelines as a marker of target organ damage.[7] However, the usefulness of carotid-femoral PWV is limited by technical complexity and cost, making it impractical in hyperacute settings like acute ischemic stroke. Estimated PWV (ePWV), a reliable surrogate for arterial stiffness, is calculated solely based on age and BP.[8] Previous study reported that ePWV has similar predictive value as measured carotid-femoral PWV.[9] Researchers from the SPRINT (Systolic Blood Pressure Intervention Trial), which investigated the cardiovascular benefits of intensive BP control in patients without diabetes, found that ePWV independently predicted outcomes, beyond the Framingham Risk Score. This underscores the importance of ePWV as marker of cardiovascular risk.[10] Other studies have consistently shown a strong association between elevated ePWV and increased stroke and mortality risk.[11,12] We previously reported an association between arterial stiffness measured by brachial-ankle PWV and poor stroke outcomes in EVT patients.[13] Therefore, ePWV may be a potential prognostic marker in patients with acute ischemic stroke undergoing EVT. However, the prognostic value of ePWV in patients with successful reperfusion by EVT remains unclear.

Using data from the OPTIMAL-BP (Outcome in Patients Treated With Intraarterial Thrombectomy–Optimal Blood Pressure Control) trial, we aim to (1) investigate the relationship between ePWV and post-EVT outcomes in patients with acute ischemic stroke; (2) assess the impact of ePWV on patients undergoing intensive versus conventional BP management following successful reperfusion; and (3) evaluate whether incorporating ePWV into the baseline risk model enhances the predictive accuracy for functional outcomes.

METHODS

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Study design

This secondary analysis leveraged data from the OPTIMAL-BP trial, a multicenter, randomized, open-label study conducted in 19 stroke centers in South Korea between June 18, 2020 and November 28, 2022. The trial compared between intensive BP and conventional BP management for 24 hours in patients with successful reperfusion by EVT for large vessel occlusion. Ethical approval was obtained from all participating institutions, and informed consent was secured from all participants (ClinicalTrials.gov Identifier: NCT04205305).[2] This secondary analysis adhered to the Strengthening the Reporting of Observational Studies in Epidemiology reporting guidelines for observational research.

Calculation of ePWV and Definition of ePWV Reduction

The ePWV was calculated using the equation derived by the Reference Values for Arterial Stiffness Collaboration,[6] as described by Greve et al.,[9] incorporating age and mean BP (MBP). The equation is as follows: $ePWV = 9.587 - 0.402 \times age + 4.560 \times 10^{-3} \times age^2 - 2.621 \times 10^{-5} \times age^2 \times MBP + 3.176 \times$

Nonstandard abbreviations and acronyms

ePWV	estimated pulse wave velocity
EVT	endovascular thrombectomy
IDI	integrated discrimination improvement
MBP	mean blood pressure
NIHSS	National Institutes of Health Stroke Scale
NRI	net reclassification improvement
OPTIMAL-BP	Outcome in Patients Treated With Intraarterial Thrombectomy–Optimal Blood Pressure Control

Clinical perspective

What Is New?

- Is estimated pulse wave velocity (ePWV), calculated using a simple equation, associated with poor outcomes in patients with successful reperfusion by endovascular thrombectomy for acute ischemic stroke?
- In this subgroup analysis of 302 patients with successful reperfusion, each1m/s increase in ePWV was associated with a 20% decrease in the likelihood of functional independence at 3 months. A reduction in ePWV within 24 hours following conventional blood pressure management increased the odds ratio forfunctional independence, and incorporating ePWV improved prognostic accuracy.

What Are the Clinical Implications?

- The ePWV has the potential to serve as a practical prognostic indicator for patients with ischemic stroke with successful reperfusion, as it can be quickly calculated using only age and blood pressure.

10^{-3} × age × MBP−1.832 × 10^{-2} × MBP. MBP was calculated as diastolic BP plus 0.4 times the difference between systolic and diastolic BP. The ePWV reduction at 24 hours after EVT was calculated as follows: ePWV reduction (%) = (ePWV at enrollment−ePWV at 24 hours) / ePWV at enrollment×100. The ePWV calculator was developed as a Google Sheets spreadsheet to enhance accessibility for all researchers (Figure 1; https://docs.google.com/spreadsheets/d/1n806eDDqR3QKeNGzNnQaj81kFr_zXTSoMpcWrmmhKsQ/edit?usp = sharing).

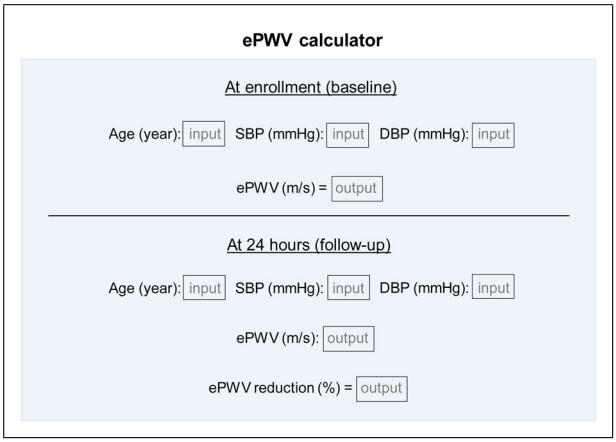

Figure 1. ePWV calculator. MBP = DBP + {0.4 × (SBP−DBP)}. ePWV = 9.587−0.402 × age + 4.560 × 10^{-3} × age^2−2.621 × 10^{-5} × age^2 × MBP + 3.176 × 10^{-3} × age × MBP−1.832 × 10^{-2} × MBP. ePWV reduction = (ePWV at baseline−ePWV at follow-up) / ePWV at baseline × 100. To facilitate ePWV calculations for all researchers, we provide a calculator accessible through Google Sheets (https://docs.google.com/spreadsheets/d/1n806eDDqR3QKeNGzNnQaj81kFr_zXTSoMpcWrmmhKsQ/edit?usp = sharing). DBP indicates diastolic blood pressure; ePWV, estimated pulse wave velocity; MBP, mean blood pressure; and SBP, systolic blood pressure.

Clinical Outcomes

Primary efficacy outcome was functional independence at 3 months, defined as a modified Rankin Scale (mRS) score of 0–2. Dependence or death was categorized as a mRS score of 3–6. Primary safety outcomes included symptomatic intracerebral hemorrhage within 36 hours and mortality related to the index stroke within 3 months. The symptomatic intracerebral hemorrhage was defined according to the European Cooperative Acute Stroke Study III as any extravascular blood in the brain or within the cranium that was linked to clinical deterioration, defined by an increase of 4 points or more in the National Institutes of Health Stroke Scale (NIHSS) score or death, and identified as the main cause of the neurologic deterioration.[14] Secondary outcomes encompassed a shift analysis of mRS scores, proportion of patients achieving excellent recovery (NIHSS score 0–1 or improvement >8 points at 24 hours), EuroQoL 5-Dimension Self-Report Questionnaire score, successful reperfusion at 24 hours (modified Thrombolysis in Cerebral Infarction grade 2b, 2c, or 3), and incidence of malignant cerebral edema within 36 hours. Malignant cerebral edema was characterized by rapidly worsening neurological status with significant brain swelling on neuroimaging.[15]

Statistical Analysis

Patient characteristics were compared across ePWV quartiles using ANOVA or Kruskal–Wallis test for continuous variables and chi-square or exact test for categorical variables. Continuous data were presented as mean±SD or median and interquartile range, and categorical data were presented as frequencies and percentages. For the analysis of the primary and secondary outcomes, binary logistic regression was used. Ordinal logistic regression was employed for a shift analysis of mRS reduction, and the association of ePWV with EuroQoL 5-Dimension Self-Report Questionnaire score was analyzed by linear regression. Multivariable regression model calculated adjusted odds ratios (ORs) and 95% CIs for outcomes per 1m/s increase in ePWV or with the first ePWV quartile as a reference. Interactions between ePWV and the covariates were explored in the multivariable regression model. A restricted cubic spline curve visualized the OR of ePWV for the primary efficacy outcome. Net reclassification improvement (NRI) and integrated discrimination improvement (IDI) assessed the predictive improvement of adding ePWV to the baseline risk model, which included important clinical variables and covariates.[2] Because systolic BP is associated with EVT prognosis and included as a variable in the ePWV equation,[9] it was also incorporated into the baseline risk model for comparison. Logistic regression analyzed the association between ePWV reduction and the primary efficacy outcome. Statistical analyses were performed with IBM SPSS Statistics software Version 27.0 (IBM, Armonk, New York, NY, USA) and SAS analytics software Version 9.4 (SAS Institute, Cary, NC, USA). Two-tailed *P* values were used, with a significance threshold of $P<0.05$.

RESULTS

Patients and Baseline Characteristics

Of the 306 patients enrolled in the OPTIMAL-BP trial, data from 302 patients with available functional outcomes at 3 months were analyzed (Figure S1). The study population consisted of 180 men (59.6%) and 122 women (40.4%) with a mean age of 73.1±11.5 years. At 3-month follow-up, 141 patients (46.7%) achieved functional independence. The ePWV values were categorized into quartiles: Q1 (<11.60 m/s, n = 75, 24.8%), Q2 (11.60–13.35 m/s, n = 78, 25.8%), Q3 (13.36–14.55 m/s, n = 74, 24.5%), and Q4 (>14.55 m/s, n = 75, 24.8%). Higher ePWV was associated with older age, women, lower body mass index, nonsmoking status, atrial fibrillation, peripheral artery occlusive disease, previous stroke, higher NIHSS score at baseline, cardioembolism stroke subtype, and prior use of antiplatelet agents, anticoagulants, and statins (Table 1). In addition, collateral was poor in patients with higher ePWV (Spearman's rank correlation coefficient between the ordinal Tan scale and ePWV quartiles −0.15; $P = 0.009$). As the ePWV values increased across quartiles, the proportion of functional independence observed after 3 months decreased ($P<0.001$; Figure 2).

Primary Outcomes

In the univariable analysis, continuous ePWV was significantly associated with functional independence at 3 months. For each 1 m/s increase in ePWV, the odds of functional independence decreased by 23% (OR, 0.77 [95% CI, 0.68–0.86]; $P<0.001$; Figure S2A). Additionally, when ePWV was categorized into quartiles, patients in the second, third, and fourth quartiles had significantly lower odds of functional independence compared with those in the first quartile (Q2: OR, 0.50 [95% CI, 0.26–0.97]; $P = 0.03$; Q3: OR, 0.38 [95% CI, 0.20–0.74]; $P = 0.004$; Q4: OR, 0.24 [95% CI, 0.12–0.47]; $P<0.001$).

In the multivariable analysis, both continuous ePWV and the fourth ePWV quartile remained independently associated with functional independence at 3 months. For each 1 m/s increase in ePWV, the adjusted odds of functional independence decreased by 20% (adjusted OR, 0.80 [95% CI, 0.68–0.94]; $P = 0.008$; Figure S2B). Compared with the first quartile, patients in the fourth quartile had significantly lower adjusted odds of functional independence (adjusted OR, 0.36 [95% CI, 0.14–0.95]; $P = 0.03$). No interaction effects were observed between ePWV and the covariates including BP management group (all *P* values for interactions≥0.05; Table 2). Meanwhile, ePWV was not associated with the primary safety outcomes, including symptomatic intracerebral hemorrhage and stroke-related death (all *P* values≥0.05; Table S1).

Secondary Outcomes

In the univariable analysis, continuous ePWV was significantly associated with both higher mRS scores (OR, 0.77 [95% CI, 0.70–0.85]; $P<0.001$) and lower quality of life as measured by EuroQoL 5-Dimension Self-Report Questionnaire scores (OR, −0.07 [95% CI, −0.09 to −0.05]; $P<0.001$). When ePWV was categorized into quartiles, patients in the second, third, and fourth quartiles exhibited significantly higher odds of worse ordinal mRS scores compared with those in the first quartile (all *P* values<0.05).

In the multivariable analysis, both continuous ePWV and the fourth ePWV quartile were independently associated with higher mRS scores (per 1 m/s increase:

Table 1. Demographic and Clinical Characteristics

	Total	Q1: <11.60	Q2: 11.60–13.35	Q3: 13.36–14.55	Q4: >14.55	*P* value
	(N = 302)	(N = 75)	(N = 78)	(N = 74)	(N = 75)	
Demographics						
Age, y	73.1±11.5	58.0±7.8	70.8±5.6	78.7±4.1	84.6±5.6	<0.001
Women	122 (40.4)	18 (24.0)	24 (30.8)	37 (50.0)	43 (57.3)	<0.001
Body mass index, kg/m^2	23.9 [21.6, 25.7]	24.8 [22.8, 26.7]	24.0 [21.9, 25.6]	23.4 [21.5, 25.4]	23.1 [20.8, 25.4]	0.01
Medical history						
Hypertension	231 (76.5)	52 (69.3)	59 (75.6)	56 (75.7)	64 (85.3)	0.14
Diabetes	127 (42.1)	27 (36.0)	32 (41.0)	29 (39.2)	39 (52.0)	0.21
Dyslipidemia	115 (38.1)	27 (36.0)	32 (41.0)	31 (41.9)	25 (33.3)	0.66
Smoking	68 (22.5)	38 (50.7)	20 (25.6)	6 (8.1)	4 (5.3)	<0.001
Atrial fibrillation	146 (48.3)	19 (25.3)	34 (43.6)	51 (68.9)	42 (56.0)	<.001
CAOD	34 (11.3)	5 (6.7)	11 (14.1)	9 (12.2)	9 (12.0)	0.50
PAOD	8 (2.6)	0 (0.0)	1 (1.3)	1 (1.4)	6 (8.0)	0.01
Previous stroke	66 (21.9)	10 (13.3)	15 (19.2)	24 (32.4)	17 (22.7)	0.03
Active cancer	14 (4.6)	4 (5.3)	5 (6.4)	2 (2.7)	3 (4.0)	0.79
Previous treatments						
Antiplatelet	76 (25.2)	10 (13.3)	18 (23.1)	24 (32.4)	24 (32.0)	0.02
Anticoagulant	48 (15.9)	4 (5.3)	15 (19.2)	16 (21.6)	13 (17.3)	0.03
Antihypertensive	153 (50.7)	34 (45.3)	34 (43.6)	41 (55.4)	44 (58.7)	0.17
Statin	87 (28.8)	8 (10.7)	27 (34.6)	29 (39.2)	23 (30.7)	0.001
Stroke subtypes						
Cardioembolism	152 (50.3)	25 (33.3)	32 (41.0)	50 (67.6)	45 (60.0)	<0.001
Large artery atherosclerosis	84 (27.8)	23 (30.7)	29 (37.2)	13 (17.6)	19 (25.3)	
Stroke of other determined etiology	5 (1.7)	2 (2.7)	1 (1.3)	1 (1.4)	1 (1.3)	
Negative evaluation	43 (14.2)	24 (32.0)	8 (10.3)	4 (5.4)	7 (9.3)	
Two or more causes	18 (6.0)	1 (1.3)	8 (10.3)	6 (8.1)	3 (4.0)	

(*Continued*)

Table 1. (Continued)

	Total	Q1: <11.60	Q2: 11.60–13.35	Q3: 13.36–14.55	Q4: >14.55	*P* value
	(N = 302)	(N = 75)	(N = 78)	(N = 74)	(N = 75)	
EVT parameters						
NIHSS score just before EVT						
0–5	32 (10.6)	10 (13.3)	8 (10.3)	8 (10.8)	6 (8.0)	0.02
6–15	162 (53.6)	47 (62.7)	49 (62.8)	32 (43.2)	34 (45.3)	
≥16	108 (35.8)	18 (24.0)	21 (26.9)	34 (45.9)	35 (46.7)	
Infarction volume, (mL)	16.9 [6.0, 52.7]	20.1 [8.4, 59.2]	14.2 [6.8, 29.4]	25.4 [5.4, 60.6]	13.8 [5.2, 62.5]	0.45
Onset to puncture time (min)	361.0 [210.5, 725.0]	357.0 [209.0, 712.5]	439.0 [226.0, 804.3]	314.0 [187.5, 620.0]	440.0 [227.0, 792.0]	0.31
Onset to randomization time (min)	480.0 [312.5, 830.0]	480.0 [317.5, 787.5]	540.0 [310.0, 900.0]	432.0 [299.0, 705.0]	540.0 [350.0, 909.0	0.28
Occlusion of the anterior circulation	249 (89.9)	62 (89.9)	67 (89.3)	62 (92.5)	58 (87.9)	0.84
ASPECTS ≥6	284 (95.0)	69 (95.8)	74 (94.9)	69 (93.2)	72 (96.0)	0.88
Good collateral (Tan scale >1)	192 (67.4)	52 (77.6)	55 (72.4)	46 (64.8)	39 (54.9)	0.02
Successful recanalization (mTICI 2b-3)	263 (92.0)	63 (90.0)	66 (86.8)	65 (94.2)	69 (97.2)	0.10
First-pass recanalization	202 (66.9)	54 (72.0)	47 (60.3)	50 (67.6)	51 (68.0)	0.48
BP management after EVT						
Conventional	147 (48.7)	37 (49.3)	39 (50.0)	34 (45.9)	37 (49.3)	0.96
Intensive	155 (51.3)	38 (50.7)	39 (50.0)	40 (54.1)	38 (50.7)	
ePWV parameters						
SBP, mmHg	150.0 [145.0, 162.0]	146.0 [142.5, 154.5]	150.5 [145.8, 167.3]	149.0 [145.0, 159.0]	159.0 [148.0, 170.0]	<0.001
DBP, mmHg	85.0 [75.5, 94.0]	81.0 [74.0, 91.0]	85.5 [73.8, 96.0]	81.0 [74.0, 91.5]	88.0 [79.0, 100.0]	0.005
MBP, mmHg	112.0 [105.6, 119.1]	108.8 [102.1, 114.7]	113.5 [106.0, 120.8]	111.8 [104.0, 116.7]	117.2 [109.6, 124.0]	<0.001
ePWV, m/s	13.1±2.2	10.2±0.9	12.6±0.5	14.0±0.4	15.7±1.0	<0.001

Continuous and categorical variables are shown as mean±SD or median (interquartile range) and number (%), respectively.

ASPECTS indicates Alberta Stroke Program Early CT Score; BP, blood pressure; CAOD, coronary artery obstructive disease; DBP, diastolic blood pressure; ePWV, estimated pulse wave velocity; EVT, endovascular thrombectomy; MBP, mean blood pressure; mTICI, modified Thrombolysis in Cerebral Infarction grade; NIHSS, National Institutes of Health Stroke Scale; PAOD, peripheral artery occlusive disease; Q, quartile; and SBP, systolic blood pressure.

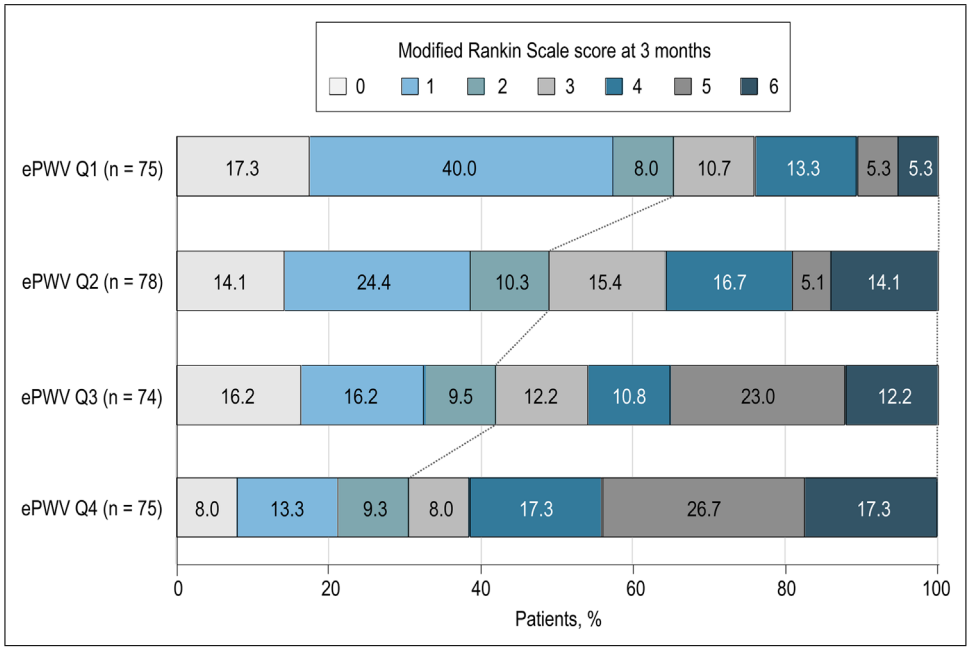

Figure 2. Distribution of the modified Rankin Scale score at 3 months by ePWV quatiles. With increasing ePWV quartiles, the proportion of patients achieving functional independence (modified Rankin Scale score 0–2) at 3 months decreased. The modified Rankin Scale score measures degree of disability (score range, 0 [symptom free] to 6 [death]). ePWV indicates estimated pulse wave velocity.

adjusted OR, 0.82 [95% CI, 0.72–0.93]; $P = 0.003$; Q4 compared with Q1: adjusted OR, 0.42 [95% CI, 0.19–0.91]; $P = 0.02$). Additionally, continuous ePWV was independently associated with a decreased likelihood of excellent recovery in the NIHSS score at 24 hours (adjusted OR, 0.82 [95% CI, 0.68–0.99]; $P = 0.04$) and lower EuroQoL 5-Dimension Self-Report Questionnaire scores (adjusted OR, −0.06 [95% CI, −0.08 to −0.03]; $P<0.001$). Meanwhile, no independent association was found between ePWV and successful reperfusion at 24 hours or malignant cerebral edema (Table 2).

ePWV Reduction Within 24 Hours

Total 75 patients (24.8%) exhibited ePWV reduction within 24 hours, which was defined as a decrease in ePWV exceeding 13.99% (ie, the fourth quartile of ePWV reduction). In the conventional BP management group, 28 patients (19.0%) showed ePWV reduction. In the intensive BP management group, 47 patients (30.3%) experienced ePWV reduction. The ePWV reduction was significantly associated with systolic BP, diastolic BP, and MBP at 24 hours in both conventional and intensive BP management groups (all P values<0.05; Table S2).

Patients with conventional BP management and ePWV reduction were most likely to achieve functional independence (78.6%), followed by conventional BP without ePWV reduction (48.7%), intensive BP with ePWV reduction (46.8%), and intensive BP without ePWV reduction (36.1%) ($P = 0.001$; Figure 3). In the conventional BP management group, those in the highest quartile of ePWV reduction were significantly more likely to achieve functional independence compared with the lowest quartile (adjusted OR, 3.41 [95% CI, 1.02–11.38]; $P = 0.04$). In contrast, no significant association was observed between ePWV reduction and functional independence in the intensive BP group (Table 3).

Prognostic Performance

To assess the prognostic value of ePWV, 3 models predicting functional independence at 3 months were developed. Model 1 served as the baseline risk model, encompassing age, sex, onset-to-randomization time, baseline NIHSS score, and BP management group. Model 2 added baseline systolic BP to Model 1, and Model 3 incorporated ePWV. The predictive performance of Model 3 was superior to Models 1 and 2, as demonstrated by the NRI and IDI metrics. For continuous ePWV, Model 3 significantly outperformed Model 1 (NRI, 0.28 [95% CI, 0.06–0.50]; $P = 0.01$; IDI, 0.02 [95% CI, 0.003–0.04]; $P = 0.01$) and Model 2 (NRI, 0.26 [95% CI, 0.04–0.49]; $P = 0.02$; IDI, 0.02 [95% CI, 0.004–0.04]; $P = 0.01$). Similarly, quartile-based ePWV showed significant improvement over Model 1 (NRI, 0.27 [95% CI, 0.07–0.47]; $P = 0.008$; IDI, 0.01

Table 2. Association of ePWV With Primary and Secondary Outcomes

	Unadjusted OR (95% CI)	*P* value	Adjusted OR (95% CI)*	*P* value	*P* value for interaction
Primary efficacy outcome					
Functional independence at 3 mo					
Continuous ePWV for each 1 m/s increase	0.77 (0.68–0.86)	<0.001	0.80 (0.68–0.94)	0.008	
Q1: <11.60 m/s	Reference		Reference		
Q2: 11.60–13.35 m/s	0.50 (0.26–0.97)	0.03	0.61 (0.26–1.47)	0.27	
Q3: 13.36–14.55 m/s	0.38 (0.20–0.74)	0.004	0.61 (0.23–1.59)	0.31	
Q4: >14.55 m/s	0.24 (0.12–0.47)	<0.001	0.36 (0.14–0.95)	0.03	
Intensive BP management group	0.54 (0.34–0.86)	0.009	0.50 (0.29–0.84)	0.009	0.40
Secondary outcomes					
mRS score reduction (shift analysis)†					
Continuous ePWV for each 1 m/s increase	0.77 (0.70–0.85)	<0.001	0.82 (0.72–0.93)	0.003	
Q1: <11.60 m/s	Reference		Reference		
Q2: 11.60–13.35 m/s	0.56 (0.32–0.99)	0.04	0.74 (0.36–1.51)	0.40	
Q3: 13.36–14.55 m/s	0.41 (0.23–0.73)	0.002	0.79 (0.37–1.72)	0.55	
Q4: >14.55 m/s	0.24 (0.13–0.43)	<0.001	0.42 (0.19–0.91)	0.02	
Excellent recovery in NIHSS score at 24 h					
Continuous ePWV for each 1 m/s increase	0.89 (0.79–1.02)	0.09	0.82 (0.68–0.99)	0.04	
Q1: <11.60 m/s	Reference		Reference		
Q2: 11.60–13.35 m/s	0.55 (0.25–1.21)	0.13	0.42 (0.15–1.19)	0.10	
Q3: 13.36–14.55 m/s	0.70 (0.33–1.50)	0.35	0.47 (0.16–1.40)	0.47	
Q4: >14.55 m/s	0.63 (0.29–1.37)	0.24	0.43 (0.14–1.30)	0.13	
EQ-5D-3L score‡					
Continuous ePWV for each 1 m/s increase	−0.07 (−0.09 to −0.05)	<0.001	−0.06 (−0.08 to −0.03)	<0.001	
Successful reperfusion at 24 h					
Continuous ePWV for each 1 m/s increase	1.19 (0.98–1.45)	0.08	1.34 (0.99–1.81)	0.06	
Q1: <11.60 m/s	Reference		Reference		
Q2: 11.60–13.35 m/s	0.77 (0.26–2.05)	0.55	0.98 (0.25–3.76)	0.97	
Q3: 13.36–14.55 m/s	1.81 (0.50–6.47)	0.36	2.37 (0.44–12.78)	0.31	
Q4: >14.55 m/s	3.83 (0.77–19.14)	0.10	5.06 (0.74–34.59)	0.09	
Malignant cerebral edema					
Continuous ePWV for each 1 m/s increase	1.02 (0.79–1.31)	0.89	0.80 (0.55–1.19)	0.27	
Q1: <11.60 m/s	Reference		Reference		
Q2: 11.60–13.35 m/s	1.97 (0.35–11.11)	0.44	2.53 (0.25–25.76)	0.43	
Q3: 13.36–14.55 m/s	3.22 (0.63–16.50)	0.16	2.23 (0.19–25.65)	0.52	
Q4: >14.55 m/s	1.00 (0.14–7.29)	1.00	0.68 (0.05–10.08)	0.78	

BP indicates blood pressure; ePWV, estimated pulse wave velocity; EQ-5D-3L, EuroQoL 5-Dimension Self-Report Questionnaire; EVT, endovascular thrombectomy; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio; and Q, quartile.

*Adjusted for age (<65 vs ≥65), sex, onset to randomization time, NIHSS score just before EVT, and intensive BP management group.

†Analyzed by univariable or multivariable ordinal regression.

‡Analyzed by univariable or multivariable linear regression.

P value for interaction was obtained between continuous ePWV and intensive BP management group.

[95% CI, 0.001–0.03]; $P = 0.03$) and Model 2 (NRI, 0.27 [95% CI, 0.07–0.47]; $P = 0.008$; IDI, 0.01 [95% CI, 0.001–0.03]; $P = 0.03$; Table 4).

DISCUSSION

In this secondary analysis of the OPTIMAL-BP trial, we found the following. First, ePWV predicted functional outcome at 3 months in patients with acute ischemic stroke with successful reperfusion by EVT. The association between ePWV and functional outcome persisted after adjusting for potential confounders without interaction effects. Second, ePWV reduction under conventional BP management was associated with good functional outcome following EVT. Third, adding ePWV to the baseline risk model improved the predictive accuracy for functional outcomes.

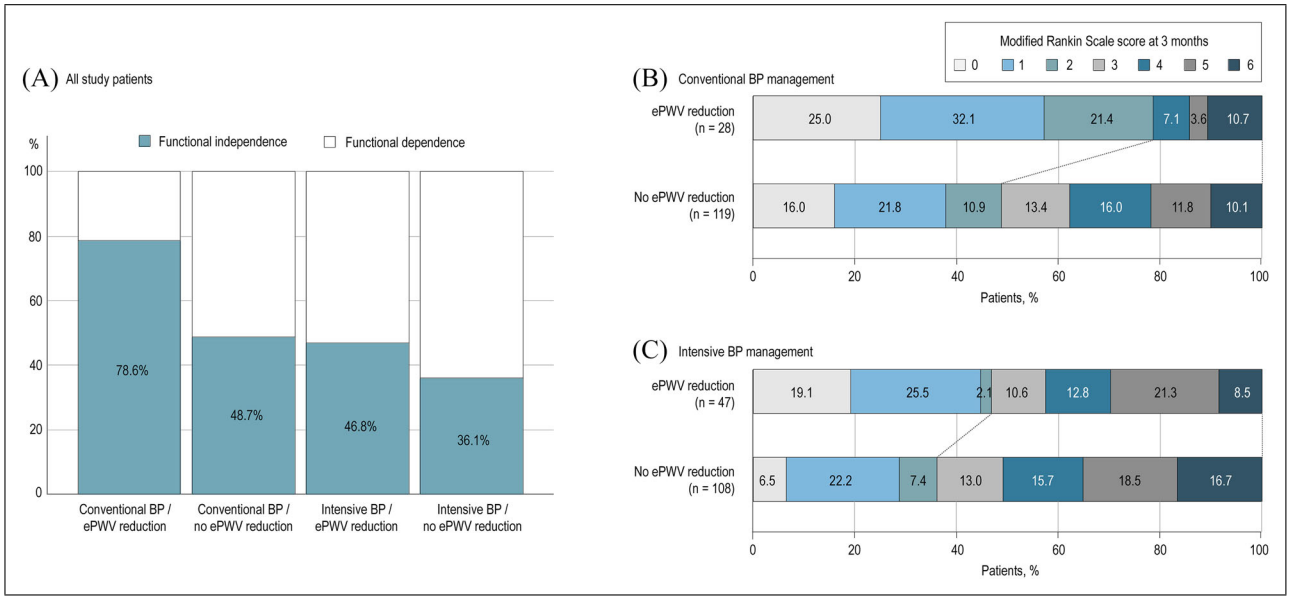

Figure 3. Combined effect of BP management and ePWV reduction on functional independence at 3 months. A, Patients with ePWV reduction demonstrated greater functional independence at 3 months compared with those without ($P = 0.001$). **B**, This effect was most pronounced in the conventional BP management group, where patients with ePWV reduction had a lower median mRS score of 1 (IQR 0–2) compared with those without (median mRS score of 3 [IQR 1–4], $P = 0.04$). **C**, In contrast, in the intensive BP management group, both patient groups exhibited similar median mRS scores: 3 (IQR 1–5) for patients with ePWV reduction and 4 (IQR 1–5) for those without, indicating no significant difference ($P = 0.07$). BP indicates blood pressure; ePWV, estimated pulse wave velocity; IQR, interquartile range; and mRS, modified Rankin scale.

Table 3. Effect of ePWV Reduction on Functional Independence at 3 Months by BP Management

	Unadjusted OR (95% CI)	*P* value	Adjusted OR (95% CI)*	*P* value
Conventional BP management				
ePWV reduction, %				
Q1: <2.66	Reference		Reference	
Q2: 2.66–8.20	0.65 (0.27–1.56)	0.33	0.60 (0.22–1.64)	0.32
Q3: 8.21–13.99	1.33 (0.55–3.23)	0.52	0.89 (0.32–2.52)	0.82
Q4: >13.99	3.67 (1.26–10.71)	0.01	3.41 (1.02–11.38)	0.04
Intensive BP management				
ePWV reduction, %				
Q1: <2.66	Reference		Reference	
Q2: 2.66–8.20	0.40 (0.14–1.09)	0.07	0.68 (0.21–2.19)	0.51
Q3: 8.21–13.99	0.42 (0.16–1.11)	0.08	0.43 (0.14–1.29)	0.13
Q4: >13.99	0.82 (0.33–2.08)	0.67	0.48 (0.16–1.42)	0.18

BP indicates blood pressure; ePWV, estimated pulse wave velocity; and OR, odds ratio.
*Adjusted for age (<65 vs ≥65), sex, onset to randomization time, and National Institutes of Health Stroke Scale score just before endovascular thrombectomy.

This study demonstrated that ePWV independently predicted 3-month functional outcomes in successfully reperfused patients with acute ischemic stroke. The findings underscore the inverse relationship between elevated ePWV and functional independence, even after adjusting for BP management strategies. The ePWV is a noninvasive method for assessing arterial stiffness that has emerged as a promising prognostic marker and risk stratification tool in cardiovascular diseases.[16] Unlike traditional risk factors, ePWV comprehensively assesses arterial wall damage, providing valuable insights into overall arterial health.[17] Notably, ePWV requires no specialized equipment and can be quickly calculated at the bedside, even in hyperacute EVT patients. Although a prior study investigated the relationship between ePWV and mortality in patients with stroke, it was not tested in patients received EVT.[18]

We hypothesized the underlying mechanisms of the association between ePWV and functional outcome at

Table 4. Prognostic Performance of ePWV for Functional Independence at 3 Months

	Improvement in predictive ability (95% CI)	*P* value
NRI		
Model 3 (continuous ePWV) vs Model 1	0.28 (0.06–0.50)	0.01
Model 3 (quantile ePWV) vs Model 1	0.27 (0.07–0.47)	0.008
Model 3 (continuous ePWV) vs Model 2	0.26 (0.04–0.49)	0.02
Model 3 (quantile ePWV) vs Model 2	0.27 (0.07–0.47)	0.008
IDI		
Model 3 (continuous ePWV) vs Model 1	0.02 (0.003–0.04)	0.01
Model 3 (quantile ePWV) vs Model 1	0.01 (0.001–0.03)	0.03
Model 3 (continuous ePWV) vs Model 2	0.02 (0.004–0.04)	0.01
Model 3 (quantile ePWV) vs Model 2	0.01 (0.001–0.03)	0.03

ePWV indicates estimated pulse wave velocity; IDI, integrated discrimination improvement; and NRI, net reclassification improvement. Model 1: age (<65 vs ≥65), sex, onset to randomization time, National Institutes of Health Stroke Scale score just before endovascular thrombectomy, and intensive blood pressure management group. Model 2: Model 1+systolic blood pressure. Model 3: Model 1+ePWV.

3 months. First, we found a link between higher ePWV and reduced collateral blood flow. Arterial stiffness frequently impairs cerebral collateral circulation through endothelial dysfunction, structural changes, and oxidative stress.[19] The presence of inadequate collaterals in individuals with elevated ePWV may have adversely affected functional outcomes. Second, arterial stiffness, marked by vessel hardening and reduced elasticity, can raise BP, disrupt blood flow, and impair cerebral autoregulation, contributing to vascular complications and delayed recovery.[20] Third, there existed the association between ePWV and established risk factors such as older age, atrial fibrillation, and coexisting vascular disease, which are known to be associated with reduced functional independence.[21] Fourth, we showed that ePWV was linked to initial stroke severity. As higher NIHSS scores frequently indicate more severe strokes and worse outcomes, higher ePWV might be associated with poor outcomes.[22] Lastly, arterial stiffness is a risk factor for prothrombotic conditions like inflammation, atherosclerosis, and sarcopenia, which may contribute to unfavorable outcome.[23,24]

Among patients with EVT, we also found that ePWV reduction was related to a higher likelihood of functional independence in patients receiving conventional BP management. This result is similar with the secondary analysis of the SPRINT, which revealed that ePWV reduction was independently associated with a decreased risk of mortality in the standard treatment group.[10] We elucidated that conventional BP management strategy targeting systolic BP of 140–180 mmHg was beneficial for patients with successful reperfusion by EVT. This is in line with the previous studies, which have shown that BP decreases within 24 hours after EVT are associated with improved cerebral autoregulation, smaller infarct volumes, and higher chances of functional independence.[25,26] However, the prognostic impact of ePWV reduction was not evident in the intensive BP management group. This may be attributed to the fact that the brain is already significantly hypoperfused due to aggressive BP control, leading to an oligemic state and limiting the potential benefits of ePWV reduction.[27] Our findings suggest that patients with elevated ePWV may warrant closer monitoring and a potentially more aggressive management approach. Furthermore, a refined approach to post-EVT BP management, targeting a systolic BP closer to 140 mmHg within the established conventional range, may also offer potential benefits in improving functional outcomes. Further research is needed to fully evaluate the potential benefits of BP control according to ePWV.

Predictive models incorporating ePWV outperformed baseline risk models using established clinical variables. Notably, although age and systolic BP are key determinants of ePWV, ePWV itself emerged as a more powerful predictor, demonstrating the potential to significantly enhance risk stratification beyond traditional clinical assessments. Our findings are consistent with earlier research, indicating that ePWV is a more effective predictor of cardiovascular events than the Framingham Risk Score in general population.[28] Furthermore, prognostic accuracy significantly increases when ePWV is integrated with traditional risk factors.[9] Traditional risk prediction models commonly require extensive clinical data and may overlook early vascular pathology. In contrast, ePWV requires only age and BP, effectively identifying early signs of vascular aging.[17] The ePWV is a practical tool for risk stratification due to its ease of calculation and strong predictive performance.

This study possess several limitations. First, the primary purpose of the OPTIMAL-BP trial did not aim to assess the impact of ePWV on post-EVT outcome. The analyses conducted were post hoc and involved small patient groups, thereby increasing the likelihood of Type 1 errors. Second, the generalizability of ePWV's impact to ethnically and genetically diverse populations remains uncertain due to the exclusively Korean study population.

CONCLUSION

In this secondary analysis of the OPTIMAL-BP trial, we demonstrated that ePWV is a predictor of poor functional outcome at 3 months post EVT in patients with acute ischemic stroke. Under conventional BP management, ePWV reduction was linked to functional independence. Given its straightforward calculation based on age and baseline BP after reperfusion, ePWV holds potential as a practical tool for risk stratification in patients with successful reperfusion after EVT.

ARTICLE INFORMATION

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Disclosures

None.

Supplemental Materials

Figure S1: Consolidated Standards of Reporting Trials diagram.
Figure S2: The restricted cubic spline curve analysis of ePWV and functional independence at 3 months.
Table S1: Association of estimated pulse wave velocity with primary safety outcomes.
Table S2: Demographic and clinical characteristics by estimated pulse wave velocity reduction Figures S1, S2.

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