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Letter to the Editor

Quantifying Venous Capacity to Evaluate Potential Cytoprotection in Acute Ischemic Stroke

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Dear Sir:

Approximately 70% of cerebral blood is stored in veins[1]; therefore, cerebral blood volume (CBV) is a surrogate of venous capacity and expresses blood availability. CBV index is a derived parameter, obtained by dividing the average CBV in Tmax >6 s region by the average CBV in normal brain tissue.[2] Quantification of blood availability in the area at risk during acute ischemic stroke (AIS) may serve as an indicator of tissue fate, although its predictive power remains underexplored, especially in patients receiving endovascular treatment (EVT). Additionally, it could reflect the availability of potential cytoprotective treatments. In recent years, many agents have been tested alongside thrombectomy through blinded administration without considering territorial blood availability, yet most have not succeeded in phase III trials.[3] This study aimed (1) to evaluate the impact of CBV index on tissue fate despite successful recanalization, comparing it with hypoperfusion index ratio (HIR) and Alberta Stroke Program Early CT Score (ASPECTS), and (2) to explore whether the CBV index could serve as a proxy for tissue blood availability, potentially informing future evaluation of drug delivery strategies.

The study design involved a single-center, retrospective analysis of prospectively collected data from adult patients who underwent EVT for proximal anterior circulation (intracranial internal carotid artery and/or M1 or proximal M2 segments of middle cerebral artery) large vessel occlusions from January 2021 to June 2024. Inclusion criteria required successful recanalization (expanded Thrombolysis in Cerebral Infarction score ≥2b50), adequate pretreatment computed tomography perfusion (CTP), and follow-up magnetic resonance imaging (MRI) within 24–48 hours. Patients with intracranial hemorrhage at baseline were excluded from the study. This study was approved by the Institutional Review Board of University of California at Los Ageles (IRB#10-001280) and conducted in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines. Demographic (age, sex), clinical (baseline modified Rankin Scale and National Institutes of Health Stroke Scale), therapeutic (intravenous thrombolysis administration), imaging (baseline ASPECTS, ischemic core, and penumbra volumes on CTP), and time interval data were collected for each patient. Additionally, CBV index and HIR were calculated based on perfusion parameters obtained from CTP acquisitions that were post-processed using RAPID software (iSchemaView, Menlo Park, CA, USA). The final ischemic lesion volume was manually segmented on the diffusion-weighted imaging sequences of MR that were previously registered to CTP slices. The outcomes of this study included ischemic lesion growth (ILG), measured as the difference between final infarct volume on MRI and baseline ischemic core volume on CTP, and considered significant if >1 mL, and the percentage of penumbra saved by the acute treatment. Spearman correlation was used to identify relationships between continuous variables, while stepwise backward regression and analysis of covariance models were applied to identify significant predictors of ILG and tissue salvage.

Ninety-nine patients met the inclusion criteria, and the main baseline characteristics of the population are summarized in Table 1 and Supplementary Figure 1. The major findings of our study indicate that, although CBV index, HIR, and ASPECTS all correlate with baseline ischemic core volume, only the CBV index

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Table 1. Baseline characteristics of study sample

Characteristics	Values (n=99)
Age (yr)	75.66±13.79
Female sex	58 (58)
mRS, median (IQR)	0 (0–1)
NIHSS	16±6.35
IVT administration	33 (33)
Last seen well to needle (min), median (IQR)	100.5 (69.3–124.8)
Last seen well to groin (min), median (IQR)	180.5 (113.8–415.5)
Door to needle (min), median (IQR)	33.0 (26.5–52.5)
Door to groin (min), median (IQR)	68.0 (51.0–90.0)
Groin to recanalization (min), median (IQR)	42.0 (28.0–56.0)
Occlusion site	
MCA	71 (72)
ICA	21 (21)
MCA+ICA	7 (7)
ASPECTS, median (IQR)	8.0 (7.0–10.0)
eTICI score	
2b50	13 (13)
2b67	21 (21)
2c	25 (25)
3	40 (40)
Perfusion imaging	
Ischemic core volume (mL), median (IQR)	3.0 (1.4–14.4)
Penumbra volume (mL), median (IQR)	67.3 (35.7–91.6)
CBV index, median (IQR)	0.8 (0.6–0.9)
HIR, median (IQR)	0.6 (0.5–0.9)

Values are presented as mean±standard deviation or n (%) unless otherwise indicated.
mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; IVT, intravenous thrombolysis; MCA, middle cerebral artery; ICA, internal carotid artery; ASPECTS, Alberta Stroke Program Early CT Score; eTICI, expanded Thrombolysis in Cerebral Infarction; CBV, cerebral blood volume; HIR, hypoperfusion intensity ratio; IQR, interquartile range.

was an independent predictor of infarct growth and the percentage of penumbra saved by EVT, even after successful recanalization (Supplementary Table 1). In fact, a higher CBV index before EVT was associated with a significantly reduced likelihood of penumbral tissue death (Figure 1), thereby limiting the growth of the baseline ischemic lesion (Figure 2). Specifically, patients with a CBV index of 0.7 or higher were less likely to experience infarct expansion, regardless of their baseline ASPECTS or HIR values. Conversely, a lower CBV index (<0.7) correlated with an increased likelihood of infarct growth, even in the presence of successful recanalization (Supplementary Figure 2).

These findings highlight the importance of venous capacity, which is often overshadowed by the focus on arterial occlusion in AIS management, and suggest that CBV index may serve as an indicator of potential tissue salvage during acute ischemia, with higher values correlating with better evolutions. Previous studies have primarily focused on functional outcomes, demonstrating that higher CBV values are associated with better prognosis in AIS[4,5]; however, they have poorly explored the impact of CBV on tissue fate, particularly in patients undergoing EVT. The lack of a significant association between ASPECTS and infarct growth, despite ASPECTS being widely used to guide treatment decisions, suggests that this score alone may not fully capture the complexities of cerebral perfusion. In contrast, our results emphasize the role of perfusion parameters over non-contrast computed tomography in predicting AIS tissue fate. When arterial inflow is successfully restored, regional venous availability appears to drive infarction evolution, regardless of baseline ASPECTS. This finding supports the beneficial effect of EVT observed in recent large-core trials.[6] Notably, CBV index outperformed HIR in predicting ILG before EVT, reinforcing the idea that these two parameters reflect distinct aspects of collateral

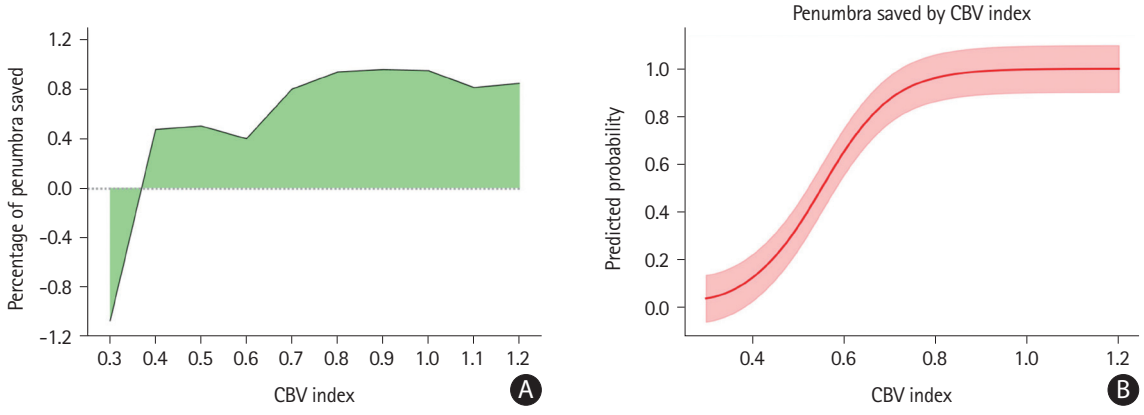

Figure 1. Association between penumbra and CBV index. (A) Line graph displaying the percentage of the tissue at risk that was saved after EVT, represented by the area under the curve. (B) Predicted probabilities from the multivariable ordinal logistic regression (proportional odds model) illustrating the relationship between baseline CBV index and the predicted probability of saving the tissue at risk. Shaded error bars represent the 95% confidence interval. CBV, cerebral blood volume; EVT, endovascular treatment.

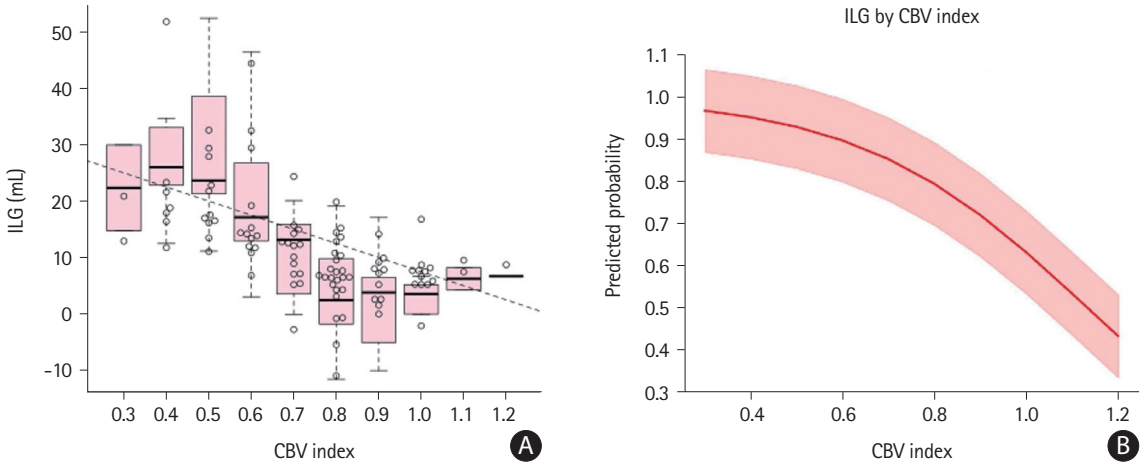

Figure 2. Association between ILG and CBV index. (A) Combined beeswarm and boxplots showing the association of the different CBV indices with absolute ILG (P<0.001). (B) Predicted probabilities from the multivariable logistic regression (model ILG >1 mL) illustrating the relationship between baseline CBV index and the predicted probability of infarct expansion. Shaded error bars represent the 95% confidence interval. ILG, ischemic lesion growth; CBV, cerebral blood volume.

flow dynamics, with venous capacity playing a dominant role in tissue perfusion in AIS via collaterals, as suggested by a *post-hoc* analysis of the Solitaire with the Intention for Thrombectomy as Primary Endovascular Treatment (SWIFT PRIME) trial.[7] The implications of these findings should be further explored in future trials. Incorporating the CBV index into treatment planning and decision-making may help clinicians better identify patients most likely to benefit from EVT, even when traditional metrics such as ASPECTS suggest a poor prognosis. Additionally, conceivably quantifying blood availability, the CBV index could help refine strategies for delivering cytoprotective drugs to hypoperfused area, potentially improving patient selection or optimizing drug dosing based on perfusion parameters. However, this study has several limitations. The retrospective design and small sample size may limit the generalizability of our findings. Furthermore, the lack of advanced perfusion imaging availability in some clinical settings poses a challenge to the widespread adoption of these parameters. Larger, multicenter studies are needed to validate our results and assess the clinical utility of CBV index in guiding AIS management.

In conclusion, our study demonstrates that the CBV index, a measure of venous capacity, is a robust predictor of tissue fate in AIS patients undergoing EVT. It provides valuable information about blood availability in hypoperfused territories and may inform future cytoprotective trials by serving as a standardized measure for drug delivery. As neuroimaging technology advances, integrating venous capacity into clinical practice may significantly enhance AIS management, ultimately leading to better patient outcomes.

Supplementary materials

Supplementary materials related to this article can be found online at https://doi.org/10.5853/jos.2025.01081.

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Conflicts of interest

Dr. Liebeskind serves as a consultant to Cerenovus, Genentech, Medtronic, Stryker, and Rapid Medical for the Imaging Core Lab. The remaining authors have no financial conflicts of interest.

Author contribution

Conceptualization: FF, DSL. Study design: FF, DSL. Methodology: FF, DSL, CL, RA. Data collection: FF, CL, RA, JF. Investigation: FF, DSL. Statistical analysis: FF. Writing—original draft: FF, DSL. Writing—review & editing: FF, DSL, CB, ME. Approval of final manuscript: all authors.

References

1. Liu L, Wu Y, Zhang K, Meng R, Duan J, Zhou C, et al. Anatomy imaging and hemodynamics research on the cerebral vein and venous sinus among individuals without cranial sinus and jugular vein diseases. *Front Neurosci* 2022;16:999134.
2. Yedavalli VS, Koneru M, Hoseinyazdi M, Marsh EB, Llinas RH, Urrutia V, et al. Low cerebral blood volume index, thrombec-

tomy, and prior stroke are independently associated with hemorrhagic transformation in medium-vessel occlusion ischemic stroke. *Stroke Vasc Interv Neurol* 2024;4:e001250.
3. Ghozy S, Reda A, Varney J, Elhawary AS, Shah J, Murry K, et al. Neuroprotection in acute ischemic stroke: a battle against the biology of nature. *Front Neurol* 2022;13:870141.
4. Li BH, Wang JH, Yang S, Wang DZ, Zhang Q, Cheng XD, et al. Cerebral blood volume index may be a predictor of independent outcome of thrombectomy in stroke patients with low ASPECTS. *J Clin Neurosci* 2022;103:188-192.
5. Sun A, Cao Y, Jia Z, Zhao L, Shi H, Liu S. Prognostic value of CBV index in patients with acute ischemic stroke treated with endovascular thrombectomy in late therapeutic window. *Front Neurol* 2024;14:1282159.
6. Kobeissi H, Adusumilli G, Ghozy S, Kadirvel R, Brinjikji W, Albers GW, et al Endovascular thrombectomy for ischemic stroke with large core volume: an updated, post-TESLA systematic review and meta-analysis of the randomized trials. *Interv Neuroradiol* 2023 Jun 28 [Epub]. Available from: http://doi.org/10.1177/15910199231185738.
7. Arenillas JF, Cortijo E, García-Bermejo P, Levy EI, Jahan R, Liebeskind D, et al. Relative cerebral blood volume is associated with collateral status and infarct growth in stroke patients in SWIFT PRIME. *J Cereb Blood Flow Metab* 2018;38:1839-1847.

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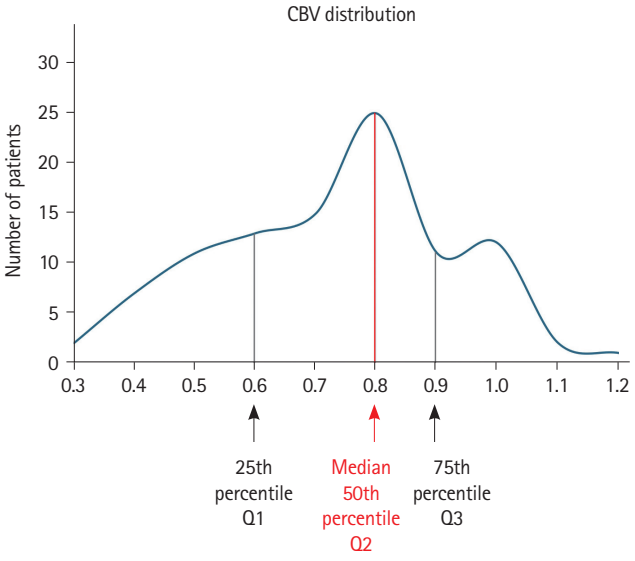
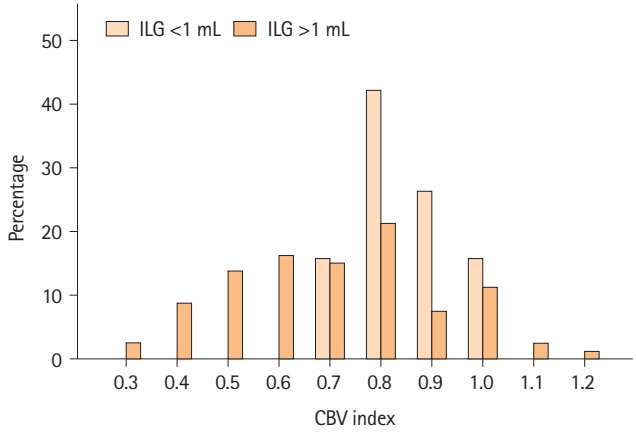
Supplementary Table 1. Predictors of ILG and saved penumbra

Linear regression	Independent variable	Unadjusted B (SE)	*P*	Adjusted B (SE)*	*P*
ILG	CBV index	-52.210 (7.991)	<0.001	-0.572 (7.899)	<0.001
	ASPECTS	-1.242 (1.110)	0.266	-0.105 (0.983)	0.244
	Penumbra volume	0.112 (0.042)	0.010	-	-
	Ischemic core volume	-0.310 (0.094)	0.001	-	-
Saved penumbra	CBV index	2.180 (0.347)	<0.001	5.802 (0.376)	<0.001
	ASPECTS	-0.012 (0.054)	0.483	-0.023 (0.048)	0.820
	Penumbra volume	0.007 (0.002)	<0.001	-	-
Logistic regression	Independent variable	OR	95% CI	*P*	
ILG >1 mL	CBV index	0.002	0.000–0.102	0.002	
	Ischemic core volume	0.955	0.919–0.993	0.019	

Statistics showing the association of independent variables and the outcomes with associated regression coefficients (B) and *P* values derived from the rank linear regression and OR and *P* values from logistic regression.
ILG, ischemic lesion growth; CBV, cerebral blood volume; ASPECTS, Alberta Stroke Program Early CT Score; SE, standard error; OR, odds ratio; CI, confidence interval.
*Adjusted for baseline characteristics, grade of recanalization, baseline perfusion volumes, and time intervals.



Supplementary Figure 1. Percentile graph showing the distribution of CBV indices among patients with 25th, 50th, and 75th percentiles. CBV, cerebral blood volume.



Supplementary Figure 2. Bar chart illustrating the frequency of ILG according to CBV indices. Note that the absence of ischemic lesion expansion was seen only when CBV index was equal to or greater than 0.7. ILG, ischemic lesion growth; CBV, cerebral blood volume.