Evaluation of Blood Brain Barrier Permeability in Early Brain Injury in Aneurysmal Subarachnoid Hemorrhage Patients: Correlation with Clinical Outcomes.

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Purpose:

Aneurysmal subarachnoid hemorrhage (SAH) is a devastating condition with high morbidity and mortality. Global cerebral edema (GCE), a main complication of SAH contributing to poor outcomes, is thought to be related to early brain injury from transient microcirculatory dysregulation, neuroinflammation and elevated neurotoxicity. Diagnosis of GCE remains challenging and currently relies on clinical examination and noncontrast CT. CT perfusion (CTP) with extended pass technique allows measurement of blood-brain barrier permeability (BBBP). Multiple parameters representing BBBP have been described, including PS (permeability surface area product), VE [volume in the extravascular extracellular space (EES)], KEP [flow rate between the EES and the intravascular space (IVS)], and Ktrans (volume transfer constant from the blood plasma to the EES). However, there is limited understanding regarding the utility of these measures of BBBP in this clinical setting. We assessed whether BBBP parameters correlate with poor clinical outcomes in SAH patients.

Materials and Methods:

IRB approval was obtained. A retrospective analysis was performed on 22 consecutive prospectively enrolled patients at our institution who underwent extended CTP on days 0-3 after aneurysmal rupture. CT perfusion scanning was performed using axial shuttle mode technique. Extended CTP data were postprocessed into BBBP quantitative maps of PS, VE, KEP and Ktrans using Olea Sphere software (Olea Medical, France). Clinical outcomes data on permanent neurologic deficit and modified Rankin scores (mRS) were collected at discharge. Univariate and multivariate analyses utilizing unpaired t tests and receiver operating characteristic (ROC)

analysis were performed to determine statistical significance.

Results:

The 22 patients were stratified based on their clinical outcomes as: 1). Permanent neurologic deficit (n = 9) and No permanent neurologic deficit (n = 13); and 2). mRS 3-6 (n = 5) and mRS 0-2 (n = 17). Clinical characteristics of the study population are shown in Table 1. PS and VE were increased in patients with poor outcomes (permanent neurologic deficit and mRS 3-6, respectively), while KEP and Ktrans were decreased (Figure 1). These results were statistically significant for all parameters. When the four parameters were combined in a multivariate ROC analysis, AUC was 0.80 for permanent neurologic deficit, and 0.89 for mRS 3-6 (Figure 2).

Conclusions:

We found significantly elevated PS in SAH patients with poor outcomes indicating increased BBBP. Furthermore, patients with poor outcomes had significantly increased VE and decreased KEP suggesting persistent interstitial edema, which has been implied in the underlying mechanism of early brain injury. Ktrans was significantly decreased in patients with poor outcomes; however, Ktrans is less reliable in this patient population since it is flow-dependent. Blood-brain barrier permeability dysregulation after SAH has not been demonstrated previously in a clinical setting. Using BBBP parameters in a multivariate analysis allows differentiation of SAH patients with poor outcomes in order to prompt early treatment intervention.

Awards:

Dyke Award
Trainee Award

Categories:

ADULT BRAIN, New Techniques/Post-processing

		Poor Outcome: Permanent Deficit (n = 9)	Favorable Outcome: No Permanent Deficit (n = 13)	p-value	Poor Outcome: mRS 3-6 (n = 5)	Favorable Outcome: mRS 0-2 (n = 17)	p-value
Mean Age (years)		52	48	0.44	51	47	0.47
Gender	Female	67% (6/9)	77% (10/13)	0.60	60% (3/5)	76% (13/17)	0.47
	Male	33% (3/9)	23% (3/13)		40% (2/5)	24% (4/17)	
Focal Deficit at presentation		33% (3/9)	23% (3/13)	0.60	80% (4/5)	71% (12/17)	0.68
Loss of Consciousness		33% (3/9)	38% (5/13)	0.81	40% (2/5)	35% (6/17)	0.85
Mean Hunt & Hess Score		2.80	2.60	0.49	3.20	2.50	0.05
Ventriculostomy Catheter		89% (8/9)	69% (9/13)	0.28	100% (5/5)	29% (5/17)	0.01
Aneurysm Location	Anterior circulation	78% (7/9)	54% (7/13)	0.25	60% (3/5)	65% (11/17)	0.84
	Posterior circulation	22% (2/9)	46% (6/13)		40% (2/5)	35% (6/17)	
Treatment	Coiled	33% (3/9)	46% (6/13)	0.55	0% (0/5)	53% (9/17)	0.03
	Clipped	66% (6/9)	54% (7/13)		100% (5/5)	47% (8/17)	

Table 1. Clinical Characteristics of the Study Population. Patients were stratified by presence of a permanent deficit (poor outcome) versus absence of permanent deficit (favorable outcome), and mRS 3-6 (poor outcome) versus mRS 0-2 (favorable outcome). P-values were calculated using Chi-square test for frequency distributions and Student t-test for mean values.

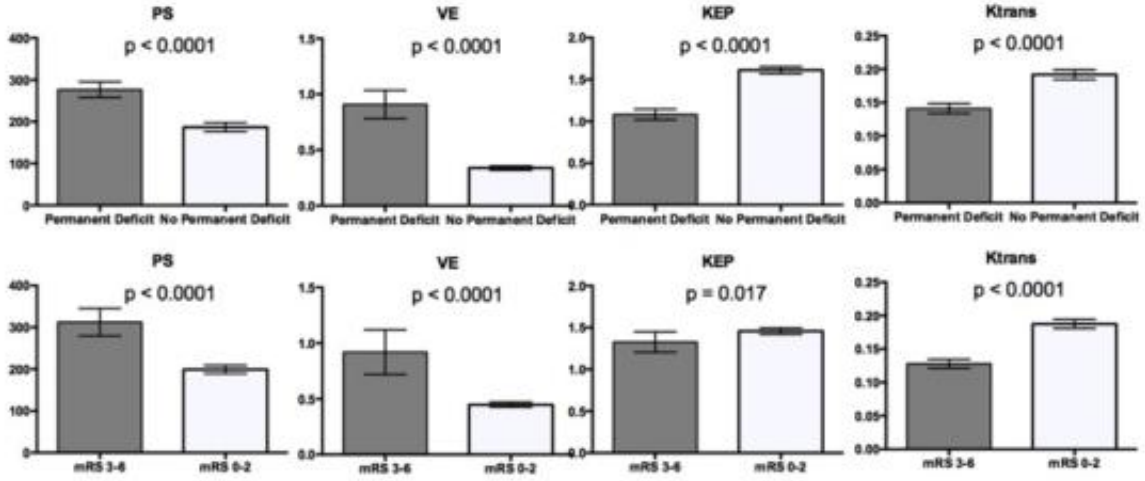

Figure 1. BBBP Parameters in SAH Patients stratified by clinical outcomes. Patients were stratified as described in the legend for Table 1.

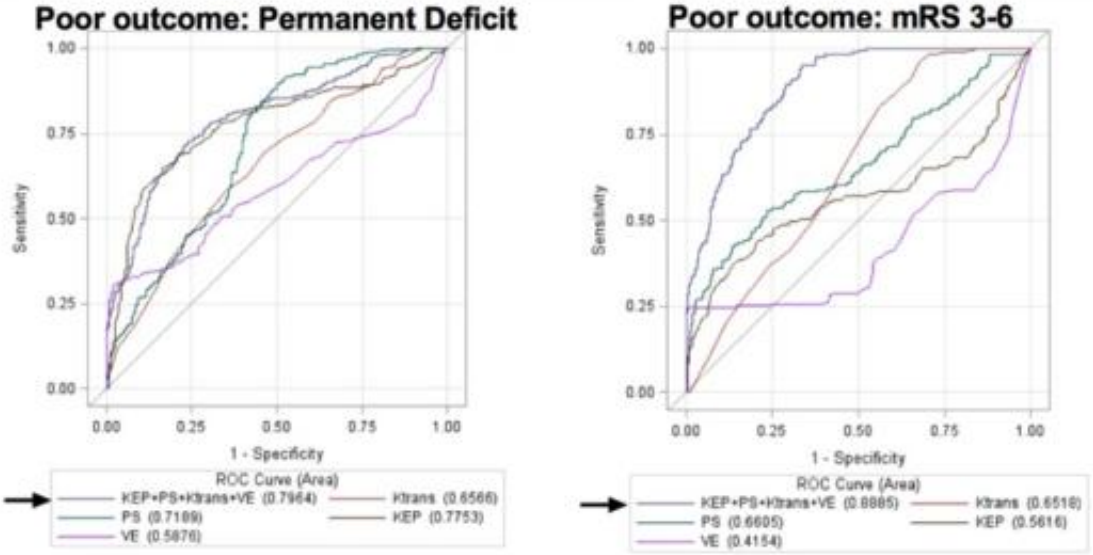

Figure 2. Univariate and Multivariate ROC Analysis of PS, VE, KEP and Ktrans in SAH Patients with Poor Clinical Outcomes compared to Patients with Favorable Cinical Outcomes.

(https://ww4.aievolution.com/asn1501/files/content/abstracts/abs_1335/FIGUREASNR2015ABSTRACT.jpg)

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