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Case Report

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Relationship of Pressure Reactivity Index and Delayed Cerebral Ischemia in Aneurysmal Subarachnoid Hemorrhage

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ABSTRACT

Patients with aneurysmal subarachnoid hemorrhage (SAH) continue to have poor functional outcome due to the occurrence of delayed cerebral ischemia (DCI). Although vasospasm represents the primary therapeutic target for mitigating DCI, DCI occurs through multifocal etiologies that involve impaired cerebral autoregulation. Worse pressure reactivity index (PRx) values, which consists of a moving correlation coefficient between intracranial pressures and mean arterial pressures, have been shown to be associated with DCI in non-randomized clinical trials.

Here, we discuss two patients that presented with high-grade SAH and comatose exams. Patient one was a 34-year-old male diagnosed with SAH from a ruptured right middle cerebral artery aneurysm. He had intact PRx values (Mean: -0.07 during hospital days 9-19), while having severe, refractory vasospasm. At the conclusion of his hospitalization, he was functionally independent, had negligible DCI, and was successfully discharged home. Patient two was a 78-year-old female diagnosed with SAH from a ruptured anterior communicating artery aneurysm. She had an improving PRx ranging from -0.1 to 0.1 early in her hospitalization. However, upon developing severe vasospasm, her PRx increased to 0.6 (overall PRx from hospital days 4-16 was 0.3), and she suffered from extensive DCI in bilateral middle cerebral and anterior cerebral artery distributions that ultimately resulted in malignant cerebral edema and brain death.

In conclusion, cerebral autoregulation as measured by PRx may represent a viable target for neuroprognostication by evaluating DCI risk in patients with SAH who develop severe or refractory vasospasm. Further studies evaluating the role of cerebral autoregulation, PRx, and its pathophysiological role in DCI are warranted.

KEYWORDS: Subarachnoid hemorrhage, Delayed cerebral ischemia, Vasospasm, Pressure reactivity index, PRx, Autoregulation, Aneurysm

INTRODUCTION

Functional outcome after aneurysmal subarachnoid hemorrhage (SAH) remains poor due to the occurrence of delayed cerebral ischemia (DCI) (7). Medical and interventional treatments for cerebral vasospasm remain the primary therapy for mitigating DCI (8). However, DCI is related to multiple factors and etiologies that include presenting clinical condition, intraventricular hemorrhage, cerebral edema (4), and impaired cerebral autoregulation (1).

The pressure reactivity index (PRx) is measured as a moving correlation coefficient between intracranial pressures (ICP) and mean arterial pressures (MAP). It evaluates cerebral autoregulation and has been shown to correlate with clinical outcome in patients with severe traumatic brain injury and SAH (3,5). However, the utility of PRx as a marker for autoregulation that correlates with DCI remains unclear due to conflicting literature (6,10).

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We report two patients with high-grade aneurysmal SAH and severe vasospasm who received continuous PRx measurements to highlight the potential role of real-time PRx evaluation in DCI.

CLINICAL PRESENTATION

Case 1

A 34-year-old male presented with a Hunt-Hess 3/ Fisher Grade 4 SAH due to a ruptured distal right middle cerebral artery (MCA) fusiform aneurysm (Figure 1A). His aneurysm was coiled on hospital day 1, and a left frontal external ventricular drain (EVD) was placed. Although initially controlled, his intracranial pressures (ICP) acutely increased on hospital day 7 with ICPs consistently greater than 30 mmHg. This refractory ICP elevation was thought to be instigated by vasospasm that was noted on computed tomography (CT) angiography and resulted in an emergent right-sided decompressive hemicraniectomy and interventional treatment of the vasospasm with intra-arterial verapamil.

Post-decompression, he remained comatose. A left frontal ICP monitor (Neurovent-PTO, Raumedic, Mills River, NC, USA) was placed for continuous ICP measurements, and he was sedated with high-dose ketamine and versed drips for elevated ICPs. Digital subtraction angiography (DSA) on hospital day 8 confirmed severe vasospasm of the right internal carotid artery (ICA) and right MCA. His vasospasm as noted by DSA appeared to improve on hospital day 10. However, he developed a second episode of prolonged severe vasospasm. This was confirmed by increasing TCD velocities and serial DSAs on hospital days 13-19. He required intra-arterial verapamil in both ICAs and MCAs and right ICA and MCA angioplasty. Despite having severe, refractory and prolonged vasospasm, his PRx remained intact (ranging from -0.3 to 0.1) during this period (Table I). At the conclusion of his serial DSAs and angiographically-confirmed severe vasospasm, follow-up magnetic resonance imaging (MRI) of his brain showed negligible DCI (Figure 2A). Sedation was weaned, and his exam improved so that he was able to be discharged to home and reach functional independence at ninety days.

Case 2

Conversely, a 78-year-old woman presented with a Hunt-Hess 4/ Fisher Grade 3 SAH due to a ruptured anterior communicating artery (Acomm) aneurysm and obstructive intraventricular hemorrhage (IVH) (Figure 1B). Her aneurysm was coiled on hospital day 1. An initial right frontal EVD was placed on hospital day 1, but stopped draining leading to a second left frontal EVD placed on hospital day 2.

Due to her comatose exam and elevated ICPs, a right frontal bolt was placed on hospital day 3. Her PRx was initially poor (0.3-0.4) on hospital days 4-5. A surveillance DSA on hospital day 6 showed mild diffuse vasospasm. By hospital day 8, an interval CT-head showed near-resolution of her IVH. This improvement in her IVH was accompanied by a PRx that improved to -0.1. However, her PRx again worsened, increasing from -0.1 on hospital day 8 to 0.4 on hospital day 10 (Table I). Due to a combination of worsening PRx and increasing TCD velocities, she was taken for DSA on hospital day 10, which confirmed severe, diffuse vasospasm that was treated with intra-arterial verapamil. Despite serial DSAs, which showed improving vasospasm by hospital day 12, her PRx continued to worsen to 0.6. An interval CT-head on hospital day 12 showed diffuse, malignant DCI in bilateral MCA and anterior cerebral artery territories (Figure 2B). Her PRx remained poor, and she progressed to brain death due to malignant herniation from her DCI.

CONCLUSION

Although evidence suggests that PRx may be predictive of functional outcome after sTBI (3) and SAH (5), the real-time association of PRx and DCI is unclear. A case study suggested

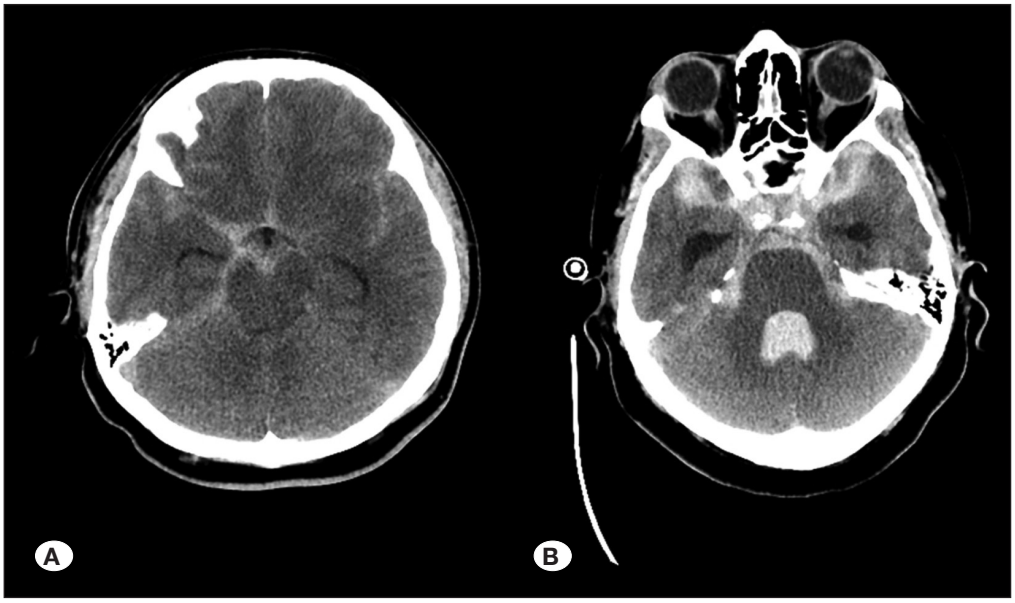

Figure 1: Initial imaging for subarachnoid hemorrhage patients: **A)** Case 1 with a right middle cerebral artery ruptured aneurysm and right frontal lobe intracerebral hemorrhage, **B)** Case 2 with an anterior communicating artery ruptured aneurysm and intraventricular hemorrhage.

Table I: Time Course of Pressure Reactivity Index Changes, Vasospasm as Noted by Digital Subtraction Angiography, and Head Imaging for Two Patients with Aneurysmal Subarachnoid Hemorrhage

	Case 1, R-MCA SAH			Case 2, Acomm SAH		
Hospital Day	**PRx**	**Vasospasm**	**Imaging**	**PRx**	**Vasospasm**	**Imaging**
1						
2						
3						
4				0.4		
5				0.3		
6				0.1	Mild diffuse	DSA
7				0		
8		Severe R-ICA/ R-MCA	DSA	-0.1		
9	-0.3			0.3		
10	-0.2	Moderate R-ICA	DSA	0.4	Severe L-ICA, R-ICA, R-VA	DSA
11	-0.1			0.5		
12	-0.3			0.6	Moderate L-ICA, R-ICA, R-VA	DSA CT-head
13	-0.1	Severe R-ICA/ R-MCA	DSA	0.2		
14	0	Severe R-ICA/ R-MCA/ R-ACA	DSA	0.3		
15	0.1	Moderate B-ICA	DSA	0.4		
16	0	Moderate B-ICA	DSA	0.5		
17	?	Moderate B-ICA	DSA			
18	0.1					
19	0	Severe R-MCA/ moderate L-ICA	DSA			
20	0.1					
21	0.1					
27			MRI-brain			

***PRx:** Pressure reactivity index, **DSA:** Digital subtraction angiography, **MRI:** Magnetic resonance imaging, **CT:** Computed tomography, **R-MCA SAH:** Subarachnoid hemorrhage due to ruptured middle cerebral artery aneurysm, **Acomm SAH:** Subarachnoid hemorrhage due to ruptured anterior communicating artery aneurysm, **ICA:** Internal carotid artery, **MCA:** Middle cerebral artery, **VA:** Vertebral artery, **?:** PRx could not be calculated due to recording error.*

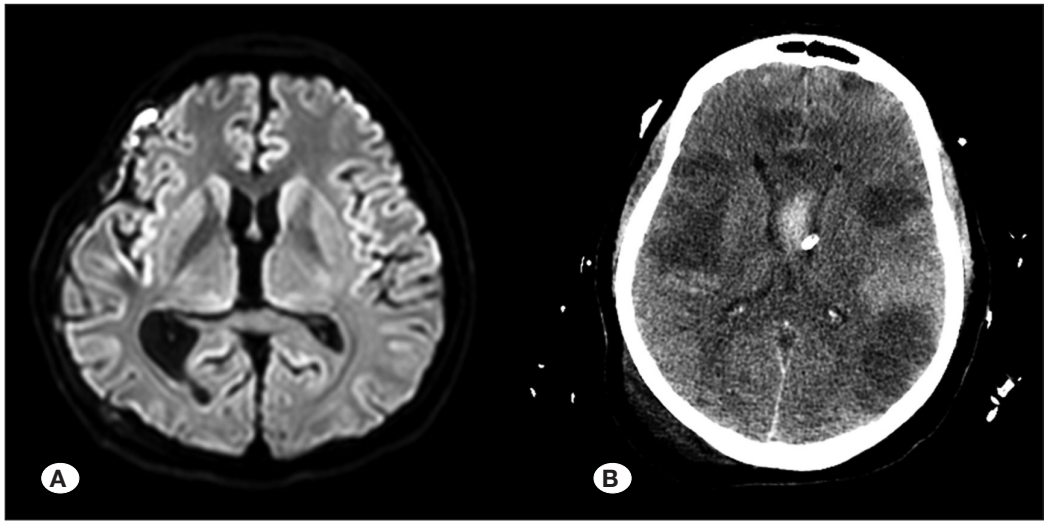

Figure 2: A) Diffusion weighted imaging sequence on magnetic resonance imaging brain for Case 1 at hospital day 27 showing negligible delayed cerebral ischemia and **B)** computed tomography head for Case 2 at hospital day 14 showing extensive delayed cerebral ischemia.

that worsening PRx values were associated with severe vasospasm, DCI, and impaired consciousness (10). A larger prospective trial found an association between worse PRx values in the first 72 hours after ictus and DCI (5). Conversely, a larger prospective study in comatose patients with SAH did not find PRx to be a significant predictor for DCI (6). However, this study utilized PRx in a more limited fashion by failing to monitor ICPs continuously. In this paper, ICPs were only measured serially at three specified intervals using a clamped EVD (6).

Our findings suggest that PRx may worsen during vasospasm and that a poor PRx may predispose a patient to developing severe DCI (Figure 3). Despite both patients undergoing a protocolized treatment for vasospasm as described earlier (2), patient two developed a rapidly worsening PRx and severe DCI that lead to malignant cerebral edema and herniation (Table I). Conversely, although patient one developed prolonged severe vasospasm that resulted in refractory ICP elevations, decompressive hemicraniectomy, and coma, his PRx remained intact during this period with an average value of -0.07 (Table I). Upon discharge, he had an intact neurologic exam and negligible DCI on imaging. Patient two started out with a poor PRx that slowly improved likely due to mild vasospasm and resolution of her obstructive hydrocephalus and intraventricular hemorrhage. However, once she developed severe vasospasm on hospital day 10, her PRx worsened from -0.1 to 0.6 with an average PRx of 0.45 (Table I). Her impaired cerebral autoregulation as suggested by her poor PRx may have contributed to her developing severe DCI that resulted in cerebral edema and brain death.

Several limitations exist before considering PRx more routinely in SAH neuroprognostication. First, there is a lack of precision when defining and measuring "autoregulation" with several different potential measurements—including ICPs, mean flow velocities from TCDs, or near infrared spectroscopy—being used to represent autoregulation. Second, PRx is not consistently defined in the literature. Several variations of PRx exist, including a "long PRx" that utilizes a moving correlation coefficient over a 20-minute window (9). In our two cases, we used the traditional definition of PRx that was calculated through a moving correlation coefficient from 30 consecutive 10-second averaged values of ICP and MAP and recorded with a Moberg CNS monitor (Micromed, Ambler, PA, USA).

We conclude that the pathophysiology of DCI and its association with vasospasm needs further study, and an improved understanding of cerebral autoregulation via PRx may represent one viable target. Further studies evaluating the role of PRx in SAH should be undertaken in the future.

AUTHORSHIP CONTRIBUTION

Study conception and design: JJC

Data collection: JJC

Analysis and interpretation of results: JJC

Draft manuscript preparation: JJC, ED

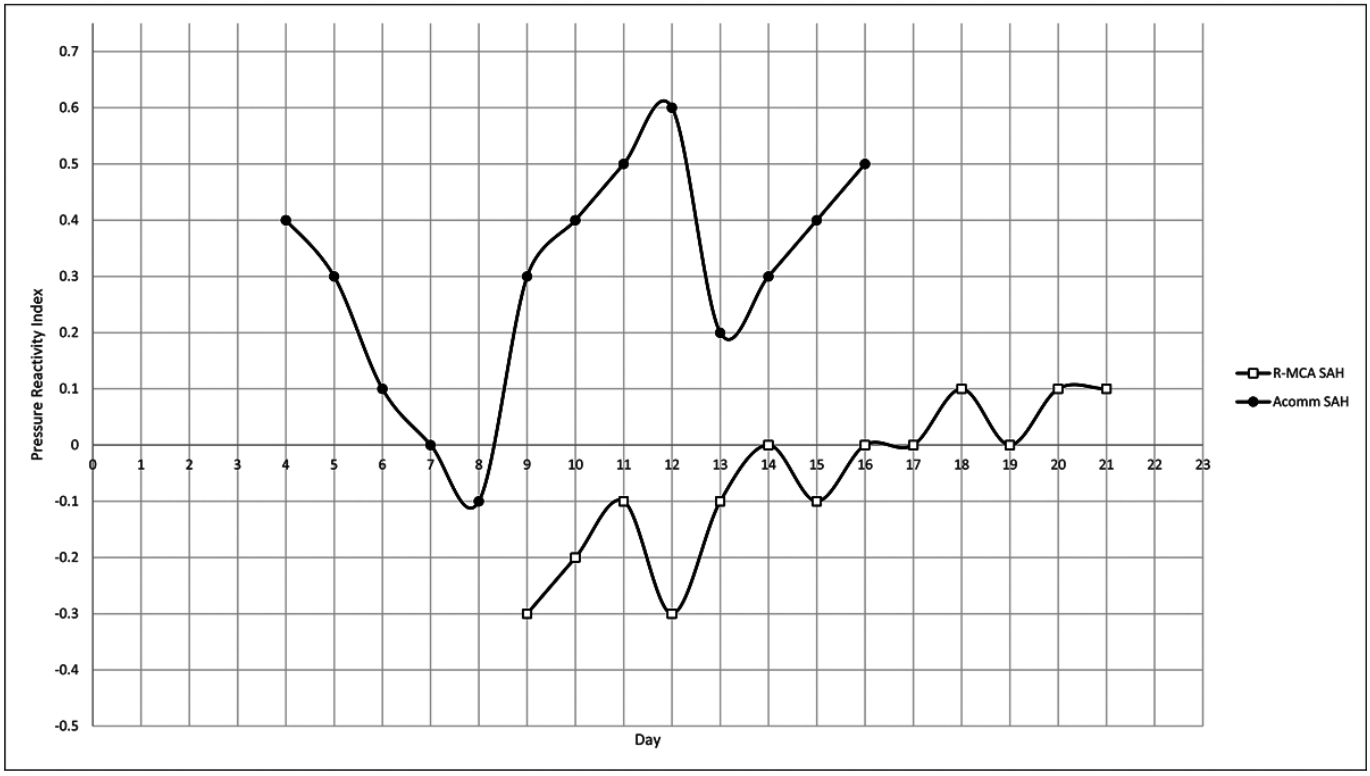

Figure 3: Pressure reactivity index vs. Time (days) for patients with SAH and vasospasm. ***R-MCA SAH:** Case 1, subarachnoid hemorrhage due to ruptured middle cerebral artery aneurysm, **Acomm SAH:** Case 2, subarachnoid hemorrhage due to ruptured anterior communicating artery aneurysm.

Critical revision of the article: JJC, ED, DRF, JCM

All authors (JJC, ED, DRF, JCM) reviewed the results and approved the final version of the manuscript.

REFERENCES

1. Calviere L, Nasr N, Arnaud C, Czosnyka M, Viguier A, Tissot B, Sol JC, Larrue V: Prediction of delayed cerebral ischemia after subarachnoid hemorrhage using cerebral blood flow velocities and cerebral autoregulation assessment. Neurocrit Care 23:253-258, 2015
2. Chang JJ, Triano M, Corbin MJ, Desale S, Liu AH, Felbaum DR, Mai JC, Armonda RA, Aulisi EF: Transcranial Doppler velocity and associations with delayed cerebral ischemia in aneurysmal subarachnoid hemorrhage. J Neurol Sci 415:116934, 2020
3. Czosnyka M, Smielewski P, Kirkpatrick P, Laing RJ, Menon D, Pickard JD: Continuous assessment of the cerebral vasomotor reactivity in head injury. Neurosurgery 41:11-17; discussion 17-19, 1997
4. Fang YJ, Mei SH, Lu JN, Chen YK, Chai ZH, Dong X, Araujo C, Reis C, Zhang JM, Chen S: New risk score of the early period after spontaneous subarachnoid hemorrhage: For the prediction of delayed cerebral ischemia. CNS Neurosci Ther 25:1173-1181, 2019
5. Gaasch M, Schiefecker AJ, Kofler M, Beer R, Rass V, Pfausler B, Thome C, Schmutzhard E, Helbok R: Cerebral autoregulation in the prediction of delayed cerebral ischemia and clinical outcome in poor-grade aneurysmal subarachnoid hemorrhage patients. Crit Care Med 46:774-780, 2018
6. Johnson U, Engquist H, Howells T, Nilsson P, Ronne-Engstrom E, Lewen A, Rostami E, Enblad P: Bedside Xenon-CT shows lower CBF in SAH patients with impaired CBF pressure autoregulation as defined by pressure reactivity index (PRx). Neurocrit Care 25:47-55, 2016
7. Kapapa T, Woischneck D, Tjahjadi M: Long-term health-related quality of life after spontaneous nontraumatic subarachnoid hemorrhage: Self and proxy reports in a 10-year period. World Neurosurg 81:105-109, 2014
8. Rabinstein AA, Friedman JA, Weigand SD, McClelland RL, Fulgham JR, Manno EM, Atkinson JL, Wijdicks EF: Predictors of cerebral infarction in aneurysmal subarachnoid hemorrhage. Stroke 35:1862-1866, 2004
9. Sanchez-Porras R, Santos E, Czosnyka M, Zheng Z, Unterberg AW, Sakowitz OW: 'Long' pressure reactivity index (L-PRx) as a measure of autoregulation correlates with outcome in traumatic brain injury patients. Acta Neurochir 154:1575-1581, 2012
10. Sugimoto K, Shirao S, Koizumi H, Inoue T, Oka F, Maruta Y, Suehiro E, Sadahiro H, Oku T, Yoneda H, Ishihara H, Nomura S, Suzuki M: Continuous monitoring of spreading depolarization and cerebrovascular autoregulation after aneurysmal subarachnoid hemorrhage. J Stroke Cerebrovas Dis 25:e171-177, 2016