Distinct Pain Trajectories Following Subarachnoid Hemorrhage are Associated with Cerebral Vasospasm and Delayed Cerebral Ischemia

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BACKGROUND

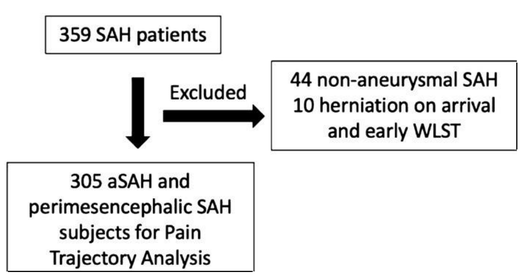
- Aneurysmal subarachnoid hemorrhage (SAH) presents with severe headache.
- We have previously described discrete pain trajectories following SAH.
- Cerebral vasospasm and delayed cerebral ischemia (DCI) are complications of acute SAH that have been linked to increased cortical spreading depolarizations. Cortical spreading depolarizations have been shown to cause pain.
- The relationship between pain trajectories following SAH and risk of vasospasm and/or DCI has not been explored

OBJECTIVES/HYPOTHESIS

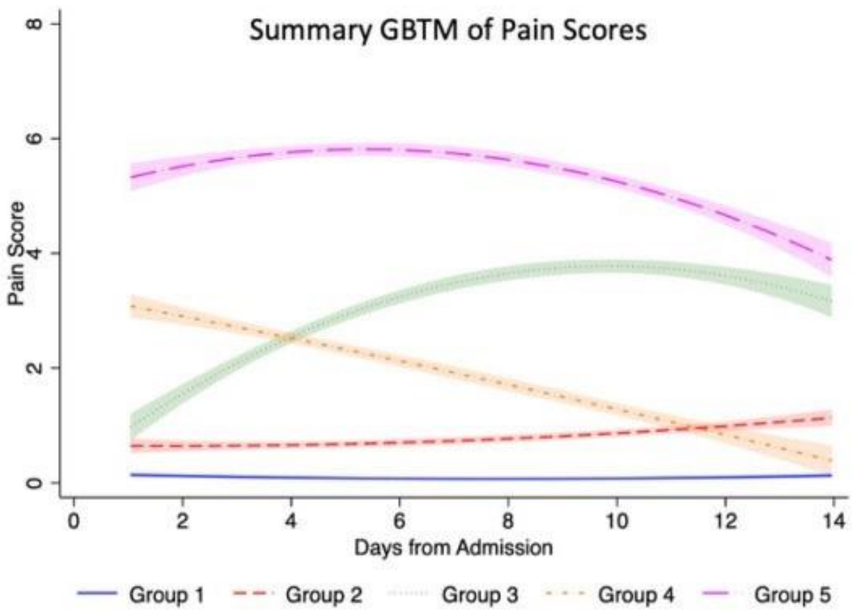
- **Objective:** Determine if inpatient pain trajectories following SAH are associated with vasospasm or DCI
- **Hypothesis:**
  - Patients reporting increased pain will have higher rates of vasospasm and DCI
  - Anterior cerebral artery (ACA) vasospasm may limit limit pain reporting

METHODS

- Retrospective review patients with aneurysmal or perimesencephalic SAH at a tertiary care NCCU from 2015-2019
- Reviewed pain scores (NRS in awake patients, MOPAT in patients unable to report scores) over fourteen days
- Group-based trajectory modeling (GBTM)
  - Finite-mixture model in which individuals are assigned to subgroups based on highest posterior group probability
- Descriptive statistics compared those in different trajectory groups
- Primary outcomes of interest were vasospasm and DCI
  - DCI defined as the development of new focal neurologic signs or a persistent decline in GCS score by 2 or more points
- Binomial logistic regression models to determine independent predictors of
- Secondary analysis looking at vasospasm location/severity



RESULTS



Pain trajectories following SAH. Summary trajectory plot demonstrating patient pain scores (NRS and MOPAT) across five different pain trajectory groups identified by group-based trajectory modeling. Pain scores are plotted over the course of the acute ICU hospitalization (14 days from admission).

A

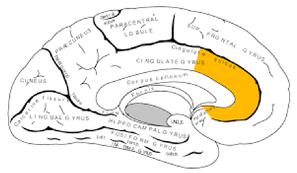
Variable	Odds Ratio	95% CI, Lower	95% CI, Upper	*p*-value
Trajectory Group				
1	2.8	1.1	7.0	0.03
2	1.7	0.72	4.1	0.23
3	1.3	0.50	3.1	0.63
4	-	-	-	-
5	3.2	1.3	8.0	0.01
Age	0.98	0.96	1.0	0.02
Hunt & Hess				
1	-	-	-	-
2	1.9	0.65	5.8	0.23
3	4.4	1.5	13.2	0.01
4	10.6	3.0	37.8	<0.001
5	1.9	0.5	7.4	0.35
Thick Blood	1.65	0.65	4.8	0.29
Prior Illicit Drug Use	1.2	0.59	2.5	0.60

B

Variable	Odds Ratio	95% CI, Lower	95% CI, Upper	*p*-value
Trajectory Group				
1	5.6	1.5	23.5	0.01
2	3.6	0.94	14.3	0.06
3	1.3	0.28	6.0	0.72
4	-	-	-	-
5	2.7	0.69	11.2	0.17
Age	0.98	0.96	1.01	0.16
Hunt & Hess				
1	-	-	-	-
2	1.7	0.34	8.5	0.51
3	1.9	0.38	9.57	0.43
4	4.8	0.90	25.3	0.06
5	1.7	0.28	10.8	0.55
Thick Blood	1.54	0.40	5.92	0.52
Prior Illicit Drug Use	1.7	0.74	4.0	0.20

Factors independently associated with vasospasm (A) and DCI (B) during hospitalization. Multivariable logistic regression of trajectory groups and covariates associated with vasospasm/DCI.

ACA Vasospasm	Group 1	Group 2	Group 3	Group 4	Group 5
Present	83.3%	86.7%	68.8%	54.5%	63%
Absent	16.7%	13.3%	31.3%	45.5%	37%



Relative rates of anterior cerebral artery vasospasm between trajectory groups after removal of patients with >24 hours of MOPAT scores.

Table 1

	TRAJECTORY GROUP					
	Group 1	**Group 2**	**Group 3**	**Group 4**	**Group 5**	**p-value**
N (%)	85 (27.9)	73 (23.9)	53 (17.4)	47 (15.4)	47 (15.4)	-
AGE, MEAN (SD)	58 (12.3)	61 (14.4)	53 (12.3)	54 (12.1)	49 (10.6)	0.23
FEMALE, N (%)	57 (67.1)	52 (71.2)	33 (62.3)	28 (59.6)	34 (72.3)	0.58
RACIAL/ETHNIC MINORITY	44 (51.8)	42 (57.5)	28 (52.8)	22 (46.8)	22 (46.8)	0.75
REPORTED ILLICIT DRUG USE	8 (9.4)	10 (13.7)	7 (13.2)	8 (17.0)	10 (21.3)	0.42
HYPERTENSION (%)	50 (58.8)	45 (61.6)	34 (64.2)	22 (46.8)	26 (55.3)	0.43
HEART DISEASE (%)	9 (10.6)	6 (8.2)	2 (3.8)	4 (8.5)	1 (2.1)	0.36
STROKE (%)	4 (4.7)	5 (6.9)	1 (2.0)	2 (4.3)	2 (4.3)	0.81
DIABETES MELLITUS (%)	13 (15.3)	8 (11.0)	13 (24.5)	6 (12.8)	6 (12.8)	0.28
HUNT-HESS SCORE, MEDIAN (IQR)	4 (3-4)	3 (2-3)	2 (2-3)	2 (2-3)	2 (2-3)	0.0001
MODIFIED FISCHER, MEDIAN (IQR)	3 (3-4)	3 (3-3)	3 (3-3)	3 (3-3)	3 (3-3)	0.0001
HYDRO/EVD, N (%)	76 (89.4)	43 (58.9)	34 (64.2)	18 (38.3)	15 (31.9)	0.0001
CRANIOTOMY, N (%)	27 (31.8)	21 (28.8)	17 (32.0)	11 (23.4)	17 (36.2)	0.73
INTUBATED, N (%)	80 (94.1)	54 (74.0)	31 (58.5)	21 (44.7)	15 (31.9)	0.0001
VASOSPASM, N (%)	53 (62.4)	29 (39.7)	20 (37.7)	13 (27.7)	27 (57.4)	0.0001
DCI, N (%)	29 (34.1)	14 (19.2)	5 (9.4)	3 (6.4)	8 (17.0)	0.0001

DISCUSSION

- Trajectory groups with the most and least pain (Group 1 and Group 5 were associated with vasospasm. Low pain trajectory group (Group 1) was associated with DCI.
- Patients in low-pain trajectories have more ACA vasospasm. ACA vasospasm may influence pain reporting.
- Pain following SAH and vasospasm/DCI may have a pathophysiologic link
- Limitations: Single center, low number experiencing DCI per trajectory group, lack of imaging to confirm delayed infarct

FUTURE DIRECTIONS

- Collaboration with University of Florida neuroICU to increase statistical power (# patients with vasospasm/DCI per trajectory group) and externally validate GBTM
- Prospective, multicenter trial describing the of pain following subarachnoid hemorrhage in the inpatient and outpatient setting