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ORIGINAL WORK

Pain Trajectories Following Subarachnoid Hemorrhage are Associated with Continued Opioid Use at Outpatient Follow-up

Matthew N. Jaffa[1,2], Ruchira M. Jha[3,4,5,6,7], Jonathan Elmer[3,4,8], Adam Kardon[1], Jamie E. Podell[1,2], Benjamin E. Zusman[4], Madeleine C. Smith[1], J. Marc Simard[9,10,11], Gunjan Y. Parikh[1,2], Michael J. Armahizer[12], Neeraj Badjatia[1,2] and Nicholas A. Morris[1,2*]

Abstract

Background: Subarachnoid hemorrhage (SAH) is characterized by the worst headache of life and associated with long-term opioid use. Discrete pain trajectories predict chronic opioid use following other etiologies of acute pain, but it is unknown whether they exist following SAH. If discrete pain trajectories following SAH exist, it is uncertain whether they predict long-term opioid use. We sought to characterize pain trajectories after SAH and determine whether they are associated with persistent opioid use.

Methods: We reviewed pain scores from patients admitted to a single tertiary care center for SAH from November 2015 to September 2019. Group-based trajectory modeling identified discrete pain trajectories during hospitalization. We compared outcomes across trajectory groups using χ^2 and Kruskal–Wallis tests. Multivariable regression determined whether trajectory group membership was an independent predictor of long-term opioid use, defined as continued use at outpatient follow-up.

Results: We identified five discrete pain trajectories among 305 patients. Group 1 remained pain free. Group 2 reported low scores with intermittent spikes and slight increase over time. Group 3 noted increasing pain severity through day 7 with mild improvement until day 14. Group 4 experienced maximum pain with steady decrement over time. Group 5 reported moderate pain with subtle improvement. In multivariable analysis, trajectory groups 3 (odds ratio [OR] 3.5; 95% confidence interval [CI] 1.5–8.3) and 5 (OR 8.0; 95% CI 3.1–21.1), history of depression (OR 3.6; 95% CI 1.3–10.0) and racial/ethnic minority (OR 2.3; 95% CI 1.3–4.1) were associated with continued opioid use at follow-up (median 62 days following admission, interquartile range 48–96).

Conclusions: Discrete pain trajectories following SAH exist. Recognition of pain trajectories may help identify those at risk for long-term opioid use.

Keywords: Chronic opioid use, Headache, Pain trajectory, Subarachnoid hemorrhage

Introduction

Subarachnoid hemorrhage (SAH) classically presents with a headache described as the worst of life [1]. Research efforts have focused on improving functional neurologic outcomes and mortality after SAH, but the characterization of pain after SAH has received less attention [2–6]. The few studies available concur that the

*Correspondence: nicholas.morris@som.umaryland.edu
[1] Department of Neurology, School of Medicine, University of Maryland, Baltimore, MD, USA
Full list of author information is available at the end of the article

headache following SAH is severe but have found disparate results regarding the temporal course of pain during the acute hospitalization [4–6]. Similar to other conditions associated with severe acute pain, SAH is associated with high rates of long-term opioid use [7, 8], a fact made more salient by the fact that the current opioid crisis in the United States is in part driven by opioid prescriptions for acute medical conditions [9].

A recent study of nonneurologic postoperative patients found that it is not simply pain severity but also the trajectory of inpatient pain that predicts important long-term outcomes [10]. It is not known if discrete inpatient pain trajectories exist following SAH. Identification of such independent pain trajectories could determine those at risk for chronic opioid use and might provide earlier opportunities for intervention.

In this study, we sought to characterize acute pain trajectories in patients hospitalized after SAH and determine whether they were associated with continued outpatient opioid use. We hypothesized that those with persistent severe pain over the course of their intensive care unit (ICU) stay would be at higher risk of continued opioid use compared with those with mild or rapidly improving pain.

Methods

Study Design

We retrospectively reviewed consecutive patients with aneurysmal or perimesencephalic SAH from November 2015 to September 2019 identified in the prospective observational Recovery After Cerebral Hemorrhage database (NCT04189471). The Recovery After Cerebral Hemorrhage database collects baseline characteristics and clinical outcomes of all patients with hemorrhagic stroke admitted to the University of Maryland Medical Center. We excluded patients with other etiologies of SAH, such as trauma, reversible cerebral vasoconstriction syndrome, or cerebral amyloid angiopathy. For our outcome analysis, we also excluded patients without outpatient follow-up.

Pain Assessment

We retrospectively reviewed patient records for all pain scores collected at 2-h intervals starting at hospital admission per nursing assessment protocols and institutional clinical standard of care. We collected patient-reported scores from 0 to 10 on the numeric rating scale (NRS) [11]. In patients unable to provide an NRS score, the multidimensional objective pain assessment tool (MOPAT) score, with physiologic-based scores ranging from 0 to 12, was collected [12]. We normalized MOPAT scores to the NRS on the basis of clinical categorization of pain severity, in which an MOPAT score of 8–12 equates to an NRS score of 7–10, both characterized as severe pain by their respective scales (Fig. 1).

Pain Management

Our standard analgesia practice started with standing acetaminophen doses up to a maximum of 4 g daily as required for pain control. We initiated opioids with 5 mg of oxycodone every 6 h as needed, with increasing doses and/or frequency based on bedside clinician evaluation of persistent pain and patient tolerance. If patients did not report adequate pain control, we added adjunctive therapies using lidocaine patches, followed by gabapentin, which was quickly uptitrated to a maximum of 1,200 mg three times daily. Forty-eight hours of high-dose dexamethasone (6 mg every 4 h) was used for persistent and refractory pain. For this study, we reviewed all analgesic agents received by patients in the medication administration reconciliation. For each day of hospitalization, the total daily dose for each medication was calculated. Opioids were converted by using a standard opioid equivalence chart and calculated as total daily oral morphine equivalents.

Outcome

Our primary outcome of interest was long-term opioid use, which we assessed using medication reconciliation completed at hospital discharge and the first outpatient neurosurgical visit. Standard medication reconciliation was completed for all medications that a patient was taking at the time of evaluation, including new prescriptions and those to be continued. If follow-up occurred greater than 6 months after admission and a visit with another physician occurred during the interim, the medication reconciliation from that visit was used instead.

Statistical Analysis

A group-based trajectory model (GBTM) is a finite mixture model that independently identifies groups who follow a similar progression of one or more repeated measures over time. The output of a GBTM typically includes polynomials that describe distinct trajectories

(See figure on next page.)

Fig. 1 Pain assessment tools. A comparison of the numeric rating scale (NRS) and multidimensional objective pain assessment tool (MOPAT). An example MOPAT scoring assessment depicts components of the physiologic and behavioral indicators of pain, as scored by bedside nursing, and the table below describes the categorization of pain severity for our institution. N/A not applicable. (Adapted from McGuire DB, Kaiser KS, Soeken K, Reifsnyder J, Keay T. Measuring pain in non-communicative palliative care patients in the acute care setting: psychometric evaluation of the multidimensional objective pain assessment tool (MOPAT) [abstract]. J Pain Symptom Manage. 2011;41(1):299–300.)

MULTIDIMENSIONAL OBJECTIVE PAIN ASSESSMENT TOOL - MOPAT

Patient Study ID: ____________________ **Nurse Study ID:**__________
Date _________ **Time:**_________

Physiologic Dimension			
Physiologic Pain Indicators	**Previous** (the most recent set of vital signs taken at least 15 minutes ago, but no longer than 4 hours ago)	**Current** (the time the MOPAT is being administered)	**Current value is likely related to pain***
Systolic Blood Pressure (mm Hg)	___ ___ ___	___ ___ ___	☐ Yes ☐ No
Heart Rate (per minute)	___ ___ ___	___ ___ ___	☐ Yes ☐ No
Respirations (per minute)	___ ___	___ ___	☐ Yes ☐ No
Diaphoresis**	☐ Absent ☐ Present ☐ Unknown	☐ Absent ☐ Present	☐ Yes ☐ No

*In your opinion, if a value in the Current column is likely related to pain, select Yes. If you think a value in the Current column is likely related to something else such as a condition or medication (e.g., fever, controlled ventilatory support, antihypertensive, vasopressor, etc.), select No.

**Diaphoresis is defined as the presence of perspiration or clamminess by observation or touch

Behavioral Dimension						
Behavioral Pain Indicators	**0 (None or Normal)**	**1 (Mild)**	**2 (Moderate)**	**3 (Severe)**	**N/A**	**Score**
Restless	Quiet	Slightly restless (fidgety)	Moderately restless (tossing/turning)	Very restless (agitated, constant movement)		
Tense Muscles (Muscle Tension)	Relaxed	Slight tenseness (Guarding)	Moderate tenseness (sensitivity or mild resistance to movement)	Extreme tenseness (stiffness or total body rigidity)		
Frowning/Grimacing (Facial Expression)	No frowning or grimacing	Slight frowning or grimacing (furrowed brow)	Moderate frowning or grimacing	Constant frowning or grimacing		
Patient Sounds (Vocalization) *Score N/A if unable to vocalize (e.g., ventilated)	Quiet	Sighs, groans, moans softly	Groans, moans loudly	Cries out or sobs		

Pain Severity	NRS	MOPAT
Mild	1-3	1-3
Moderate	4-6	4-7
Severe	7-10	8-12

Fig. 1 (See legend on previous page.)

over time (with associated confidence bands), trajectory group sizes, and individuals' trajectory group memberships. We constructed GBTMs that summarized trajectories of pain scores over time from hospital day 2 to hospital day 14, representing the typical ICU stay for our patients with SAH. We excluded day 1 data because of a high rate of missing data, as pain scores were not assessed while patients underwent aneurysm securement. We used Bayesian and Akaike information criteria to determine the optimal number of trajectory groups in our cohort and eliminated statistically insignificant higher-order polynomial terms to develop a parsimonious GBTM [13–17].

We compared outcomes across trajectory groups using the χ^2 or Fisher's exact test for categorical variable and the Kruskal–Wallis test for ordinal variables. To determine whether trajectory group membership was an independent predictor of outcome, we used logistic regression, adjusting for clinically relevant covariates selected a priori on the basis of previously reported data from this patient cohort: race/ethnicity, a history of depression, a history of opioid use, craniotomy, and insurance type [7]. We evaluated goodness of fit using a Hosmer–Lemeshow test. We used Stata version 15.0 (StataCorp, College Station, TX).

In a sensitivity analysis, we excluded patients with 24 h or more of consecutive MOPAT scores during the first 4 days of hospitalization given inherent limitations of the physiologic dimensions of the score due to influence from external factors, including hyperthermia and use of vasoactive medications, compared with patient-reported scores [12]. Sensitivity analysis was also completed after we excluded patients with perimesencephalic SAH given its separate pathophysiology from aneurysmal SAH and possible differences in headache patterns.

Data Availability

Anonymized study data will be available to qualified investigators from the corresponding author on reasonable request.

Results

We identified 305 patients eligible for inclusion in the trajectory analysis after excluding 44 patients with nonaneurysmal, nonperimesencephalic SAH and 10 who had early withdrawal of life-sustaining treatment. After we excluded an additional 48 patients lacking outpatient follow-up, 257 were left for analysis of long-term opioid use (Fig. 2). We identified five distinct pain trajectory groups (Fig. 3). The mean posterior probability of group membership was greater than or equal to 0.90, indicating that most patients could be assigned to a single trajectory group with confidence [12]. Group 1 included 85 patients (27.9% of total cohort) and remained essentially pain free throughout the studied time period. Group 2 included 73 patients (23.9% of total cohort) and reported low pain scores with intermittent spikes and an overall slight increase over time. Group 3 included 53 patients (17.4% of the total cohort) and reported dramatically increasing pain severity through day 7 with subsequent milder improvement in pain scores until day 14. Group 4 included 47 patients (15.4% of the total cohort) and experienced maximum pain immediately following admission with a steady decrement in pain scores over time. Finally, Group 5 also included 47 patients (15.4% of the total cohort) and reported moderate pain severity with slight abatement over time.

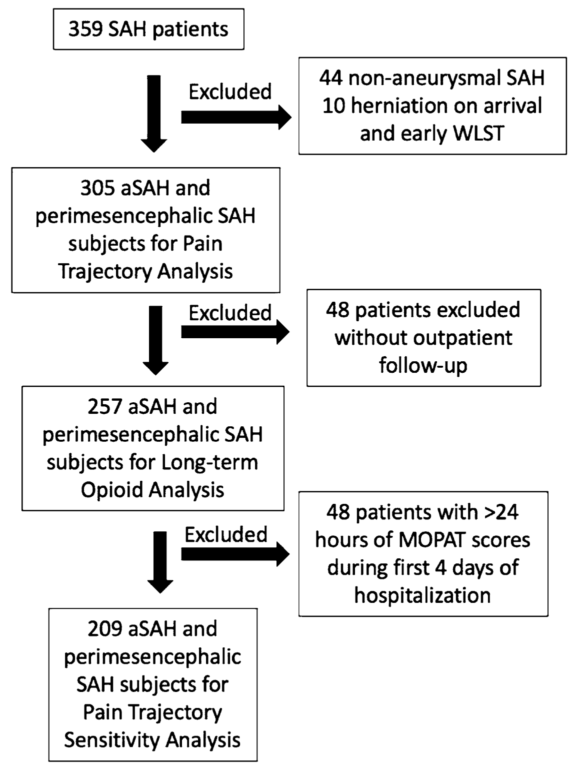

Fig. 2 Inclusion/exclusion flowchart. aSAH aneurysmal subarachnoid hemorrhage, MOPAT multidimensional objective pain assessment tool, SAH subarachnoid hemorrhage, WLST withdrawal of life-sustaining treatment

Group Demographics and Clinical Characteristics

Groups were roughly similar in terms of age, sex, race, and prior use of opioids or illicit drugs (Table 1). Rates of hypertension, heart disease, and diabetes mellitus were also similar across trajectory groups. Groups 3 and 5 had the highest rates of premorbid depression, whereas group 1 had the lowest rate.

The median Hunt–Hess score, determined at the time of admission to the hospital, was higher in groups 1 and 2 compared with the other groups. Fewer patients in trajectory groups 4 and 5 underwent intubation or EVD placement for hydrocephalus, whereas a consistent percentage of patients in each group underwent craniotomy. Groups 3 and 5 had the highest mean daily opioid doses and were more likely to have received steroids for refractory headache.

Association with Continued Opioid Use at Follow-up

In the multivariable analysis, trajectory group 3 (odds ratio [OR] 3.5; 95% confidence interval [CI] 1.5–8.3), trajectory group 5 (OR 8.0; 95% CI 3.1–21.0), history of depression (OR 3.6; 95% CI 1.3–10.0), and racial/ethnic minority (OR 2.3; 95% CI 1.3–4.1) were associated with continued opioid use at follow-up (Fig. 4). In a sensitivity analysis of 209 patients with no more than 24 h of physiologic-based pain scores, results were unchanged. Similarly, the sensitivity analysis excluding 26 patients with perimesencephalic SAH demonstrated unchanged results.

Discussion

In this study of subarachnoid hemorrhage, we identified five distinct trajectories of pain. Two of the trajectory groups, characterized by either moderate but persistent pain or dramatically increasing pain over the first seven days of hospitalization, were associated with long-term opioid use, defined as continued opioid use at outpatient follow-up. Craniotomy and a history of depression were also associated with long-term opioid use.

This analysis characterized previously unrecognized trajectories in pain following SAH. Prior studies of the longitudinal course of headache following SAH have either found headache to demonstrate increasing severity over the first 7 days, similar to our group 3 [6], or be severe and persistent during the first 14 days [4, 5]. This study is the first to decipher distinct pain trajectories for different patient groups. It is possible that the disparate results in prior studies are a result of disproportionate contributions from one trajectory group to the respective cohorts. Nonetheless, these findings are consistent with those from other acute injuries that show refractory pain to be a risk factor for chronic opioid use disorder [18–21].

Importantly, this study demonstrates that even persistent moderate pain during hospitalization following SAH is associated with continued opioid use at outpatient follow-up. Furthermore, the importance of pain trajectory is highlighted by the discrepant outcomes of groups 3 and 4. Group 4 complained of more pain than group 3 during the early acute phase, but their pain subsided either naturally or as a response to analgesic therapy, and they were much less likely to continue using opioids at outpatient follow-up. In contrast, group 3's pain increased over time and led to escalating treatments (including steroids) for refractory pain. Although their initial pain scores were low, nearly three of four patients in group 3 continued to use opioids at outpatient follow-up. We have previously reported that persistent, poorly controlled pain during hospitalization was the major contribution to the continuation of opioid use in patients treated for SAH [7]. Early recognition of high-risk patient trajectories may inform multimodal analgesic strategies aimed at reducing pain, limiting postacute opioid prescriptions, and preventing chronic opioid use. It may also help enrich future research studies for patients most likely to benefit from interventions that limit chronic opioid use.

Although baseline characteristics did not show any significant differences between trajectory groups, patients assigned to group 5 were of younger average age and had a slightly increased rate of reported depression. Interestingly, they were also noted to have higher premorbid rates of use of nonopioid analgesics, alcohol, and opioids (on the basis of self-report and toxicology screen results at admission). Similar to group 3, the mean daily analgesic dose was significantly greater than that among patients assigned to groups 1, 2, and 4. Additionally, we note higher rates of rescue steroid therapy in both groups 3 and 5, suggesting that persistent or worsening experience of pain refractory to standard analgesia plays a role in the continued use of opioids following discharge.

More than half of patients (groups 1 and 2) experienced little or no pain. These patients were less likely to use opioids at outpatient follow-up. Notably, these patients had higher Hunt–Hess scores, associated with alterations in mental status and higher rates of intubation. It is possible that pain scores in these patients are confounded by impairments in abilities to explicitly report experienced pain; however, in our sensitivity analysis excluding those patients who did not regain consciousness to a degree allowing them to report their pain using the NRS, the

(See figure on next page.)

Fig. 3 Pain trajectories following SAH. Summary trajectory plot demonstrating patient pain scores across five different pain trajectory groups identified by group-based trajectory modeling. Plots of individual trajectory cohorts display individual variance for each trajectory. Pain scores are plotted over the course of acute ICU hospitalization (14 days following admission). Day 1 values were excluded because of the number of missing values, which represented time patients were not assessed during aneurysm securement. GBTM group-based trajectory model, ICU intensive care unit, SAH subarachnoid hemorrhage

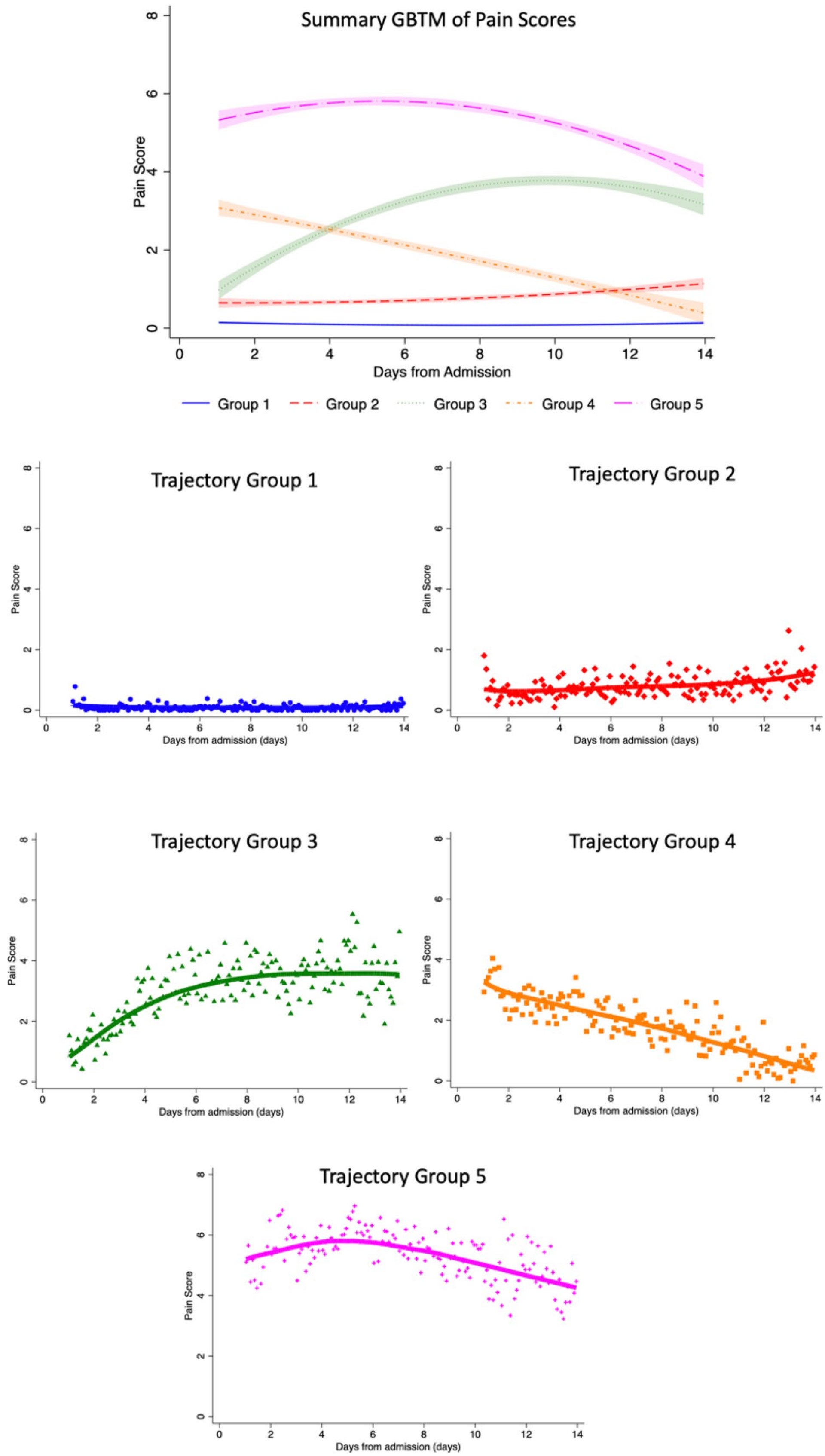

Fig. 3 (See legend on previous page.)

Table 1 Patient characteristics and unadjusted clinical outcomes

	Trajectory cohort					p-value
	Group 1	Group 2	Group 3	Group 4	Group 5	
n (%)	85 (27.9)	73 (23.9)	53 (17.4)	47 (15.4)	47 (15.4)	–
Demographics						
Age, mean (SD)	58 (12.3)	61 (14.4)	53 (12.3)	54 (12.1)	49 (10.6)	0.23
Female sex, *n* (%)	57 (67.1)	52 (71.2)	33 (62.3)	28 (59.6)	34 (72.3)	0.58
White, *n* (%)	41 (48.2)	31 (42.5)	25 (47.2)	25 (53.2)	25 (53.2)	0.75
Racial/ethnic minority, *n* (%)	44 (51.8)	42 (57.5)	28 (52.8)	22 (46.8)	22 (46.8)	–
Private Insurance, *n* (%)	51 (60.0)	38 (52.1)	34 (64.2)	29 (61.7)	35 (74.5)	0.18
Medicare/Medicaid insurance, *n* (%)	34 (40.0)	35 (47.9)	19 (35.8)	18 (38.3)	12 (25.5)	–
History						
Reported opioid use	3 (3.5)	6 (8.2)	6 (11.3)	3 (6.4)	4 (8.5)	0.45
Non-opioid analgesic use (%)	14 (16.5)	18 (24.7)	11 (20.8)	9 (19.2)	15 (31.9)	0.31
EtOH use (%)	18 (21.2)	18 (24.7)	14 (26.4)	16 (34.0)	18 (38.3)	0.22
Reported illicit drug use (%)	8 (9.4)	10 (13.7)	7 (13.2)	8 (17.0)	10 (21.3)	0.42
Depression (%)	3 (3.5)	8 (11.0)	6 (11.3)	5 (10.6)	8 (17.0)	0.10
Anxiety (%)	4 (4.7)	8 (11.0)	6 (11.3)	5 (10.6)	5 (10.6)	0.50
Any opioids (reported or positive toxicology screen results) (%)	11 (12.9)	8 (11.0)	5 (9.4)	8 (17.0)	13 (27.7)	0.07
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
Indicators of severity						
Hunt–Hess score, median (IQR)	4 (3–4)	3 (2–3)	2 (2–3)	2 (2–3)	2 (2–3)	0.0001
modified Fisher scale, median (IQR)	3 (3–-4)	3 (3–-3)	3 (3–-3)	3 (3–-3)	3 (3–-3)	0.0001
Hydrocephalus requiring EVD, *n* (%)	76 (89.4)	43 (58.9)	34 (64.2)	18 (38.3)	15 (31.9)	< 0.0001
Intubated, *n* (%)	80 (94.1)	54 (74.0)	31 (58.5)	21 (44.7)	15 (31.9)	< 0.0001
Surgical intervention						
Craniotomy, *n* (%)	27 (31.8)	21 (28.8)	17 (32)	11 (23.4)	17 (36.2)	0.73
Analgesia						
Mean daily acetaminophen dose (SD) (mg)	1496 (905)	1064 (674)	1472 (686)	1427 (859)	1877 (764)	< 0.0001
Median daily opioid dose, mg, morphine equivalents (IQR) (mg)	15.8 (4.8–-66.7)	6.7 (4.4–-22.6)	30.3 (19.4–-49.6)	15.4 (8.2–-28.1)	53.0 (37.2–-67.7)	0.0001
Steroid Tx, *n* (%)	23 (27.1)	27 (37.0)	31 (58.5)	25 (53.2)	41 (87.2)	< 0.0001
Disposition						
Home (%)	6 (7.1)	24 (32.9)	33 (62.6)	36 (76.6)	41 (87.2)	< 0.0001
Rehab facility (%)	59 (69.4)	42 (57.5)	19 (35.8)	11 (23.4)	5 (10.6)	–
Skilled nursing facility (%)	2 (2.4)	1 (1.4)	0	0	0	–
Hospice/deceased (%)	18 (21.2)	6 (8.2)	1 (1.9)	0	1 (2.1)	–
Outcomes						
Opioid Rx at discharge, *n* (%)	21 (24.7)	29 (39.7)	39 (73.6)	27 (57.5)	39 (83.0)	< 0.0001
Time from admission to follow-up, days, median (IQR)	85.5 (63–-124)	63 (48–-101)	55 (45–-76)	52.5 (45–-72)	56.5 (44–-78)	0.0001
Continued opioid use at follow-up, *n* (%)	19 (31.7)	20 (32.8)	29 (63.0)	19 (41.3)	35 (79.6)	< 0.0001

EtOH, alcohol; EVD, external ventricular drain; IQR, interquartile range; Rx, prescription; SD, standard deviation; Tx, treatment

results did not change. Treatments used to promote ventilator synchrony may also interrupt central nociceptive circuits and limit central sensitization that would otherwise contribute to long-term opioid use [22]. Indeed, patients with acute brain injury may be particularly vulnerable to central sensitization processes [23].

A history of depression and being of the racial/ethnic minority were risk factors for continued opioid use at

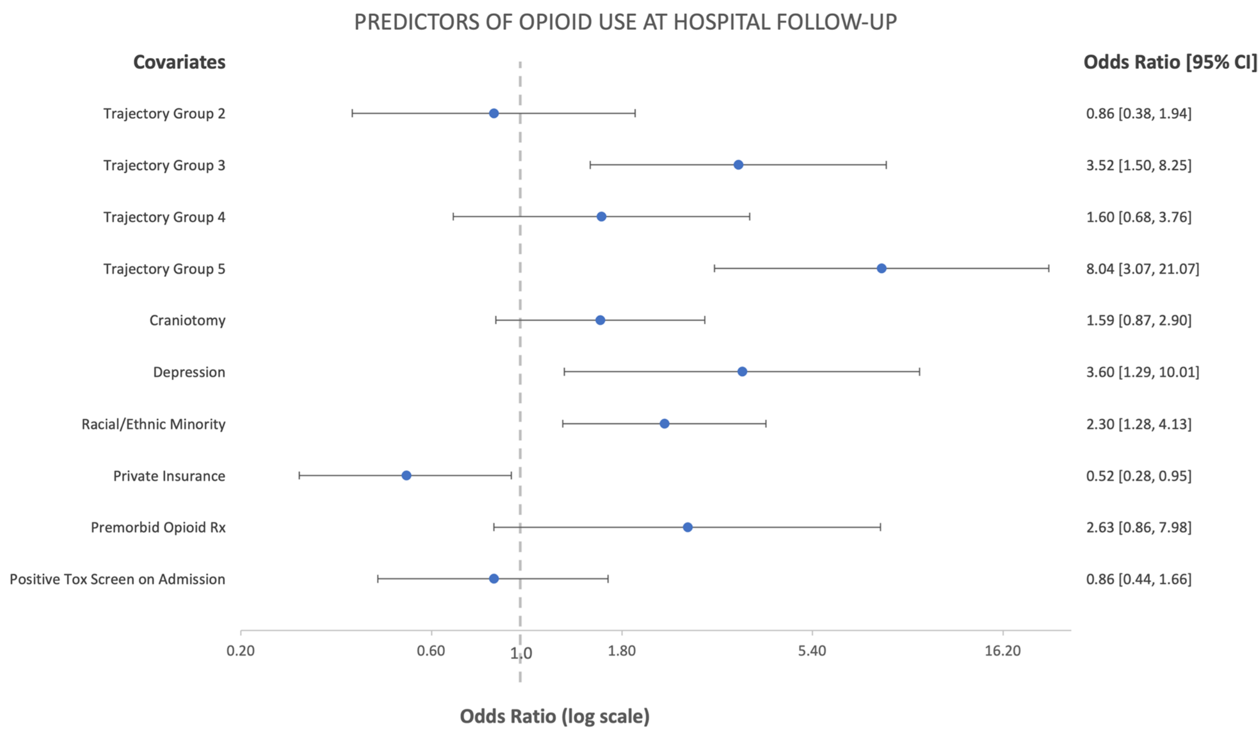

Fig. 4 Predictors of opioid use at hospital follow-up. Multivariable analysis of trajectory groups and a priori identified covariates associated with continued opioid use following hospitalization for SAH, expressed as a forest plot. CI confidence interval, Rx prescription, SAH subarachnoid hemorrhage Tox toxicology

outpatient follow-up. These factors have previously been strongly linked to chronic opioid use following surgery and intensive care, which further strengthens the validity of the results of this study [24, 25].

Several pertinent limitations to this study merit noting. Principle among these is that the analysis was limited to a retrospective review of a single center, limiting its generalizability to other patient populations with SAH. Sample size limitations significantly restrict statistical comparisons between trajectory groups, and larger studies powered to discern differences between groups may better define differences among groups. Reliance on physiologic signs of pain in patients who are intubated does not account for self-reported pain as experienced by the patient and, therefore, may undervalue its severity. Nonetheless, our findings were identical in the subset of patients who were able to report all pain scores. It may also be challenging for clinicians to categorize patients into trajectory groups in real time, limiting clinical applicability of these cohorts. However, it may be possible to recognize patients in groups 3 and 5 by their increase in pain scores over the first several days and failure to achieve pain control over the same period. Of important note, although the pain described by patients with SAH most commonly reflected headache, retrospective review of pain scores prevented differentiation by location or character.

Additional limitations relating to the analysis of continued opioid use must be discussed. It is noted that the median follow-up time for this study was 2 months, whereas 3 months usually defines chronic opioid use [9]. Additionally, determining long-term opioid use on the basis of outpatient medication reconciliation may be prone to inaccuracy. However, self-reported opioid use likely underestimates true chronic opioid use [26]. Finally, 48 patients were excluded from this additional analysis as a result of loss to follow-up, 50% of whom were deceased or transferring to hospice at the time of discharge. Among excluded patients, those assigned to trajectory groups 1 and 2 were the majority, not dissimilar to the makeup of the cohort as a whole.

Conclusions

We present a novel depiction of pain trajectories experienced following SAH in the ICU. Among these trajectory groups, evidence of even persistent moderate pain prior to discharge, as well as escalating pain and history of depression, predicts continued opioid use at hospital follow-up. Early recognition of pain trajectories may assist in identifying patients at high risk for continued opioid use at outpatient follow-up.

Author details
[1] Department of Neurology, School of Medicine, University of Maryland, Baltimore, MD, USA. [2] Program in Trauma, R Adams Cowley Shock Trauma Center, Baltimore, MD, USA. [3] Department of Critical Care Medicine, School of Medicine, University of Pittsburgh, Pittsburgh, PA, USA. [4] Department of Neurology, School of Medicine, University of Pittsburgh, Pittsburgh, PA, USA. [5] Department of Neurosurgery, School of Medicine, University of Pittsburgh, Pittsburgh, PA, USA. [6] Safar Center for Resuscitation Research, School of Medicine, University of Pittsburgh, Pittsburgh, PA, USA. [7] Clinical and Translational Science Institute, School of Medicine, University of Pittsburgh, Pittsburgh, PA, USA. [8] Department of Emergency Medicine, School of Medicine, University of Pittsburgh, Pittsburgh, PA, USA. [9] Department of Neurosurgery, School of Medicine, University of Maryland, Baltimore, MD, USA. [10] Department of Pathology, School of Medicine, University of Maryland, Baltimore, MD, USA. [11] Department of Physiology, School of Medicine, University of Maryland, Baltimore, MD, USA. [12] Department of Pharmacy Services, University of Maryland Medical Center, Baltimore, MD, USA.

Author contributions
All listed authors have made substantial contributions to the content of this manuscript, including conception and design of the study, acquisition of data, or data analysis and interpretation. Additionally, all have granted permission to submit for publication. Statistical analysis was conducted by JE and BEZ.

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Declarations

Conflicts of interest
RMJ reports funding from the National Institutes of Health National Institute of Neurological Disorders and Stroke through grants K23NS101036 and 1R01NS115815 during the conduct of the study. JE discloses funding from the National Institute of Neurological Disorders and Stroke through grants K23NS097629 and R01NS119825 during the conduct of the study. NB reports grants from the National Institutes of Health National Institute of Neurological Disorders and Stroke, from the US Department of Defense, and from the Maryland Industry Partnerships outside the submitted work. NAM and MJA report funding from the University of Maryland Baltimore Institute for Clinical and Translational Research Accelerated Translational Incubator Pilot grant, a subaward from National Center for Advancing Translational Sciences grant 1UL1TR003098, during the conduct of the study. The other authors declare no conflicts of interest.

Ethical approval/informed consent
Data used in this study were obtained via our institutional review board-approved observational study of recovery following cerebral hemorrhage (HP-00056063). For this study, formal consent was not required by our local institutional review board.

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