


RESEARCH

Open Access



Postoperative fever and clinical outcomes after endoscopic surgery for spontaneous intracerebral hemorrhage: a retrospective database study

Shuang Liu^{1†}, Yunjian Zhang^{2†}, Shengyang Su^{3†}, Jirao Ren³, Jinyong Long³, Shikui Cao³, Fuhua Li³, Zihui Gao³, Deqiang Wang⁴ and Xiaobiao Zhang^{1*} 

Abstract

Background Spontaneous intracerebral hemorrhage (SICH) is a severe stroke with high mortality and disability rates. Endoscopic surgery is an increasingly widely used minimally invasive method for the treatment of SICH. However, the impact of fever on patient outcomes remains unclear.

Methods We retrospectively included patients aged 18 years or older with supratentorial SICH confirmed by CT, who underwent endoscopic hematoma evacuation within 48 h of symptom onset. The primary outcome was the modified Rankin Scale (mRS) score at 3 months. Secondary outcomes included hospital and neurosurgical intensive care unit (NSICU) stays, and perioperative complications. We analyzed the association between postoperative fever (highest temperature within 24 h after surgery) and these outcomes using multivariate analysis, generalized additive models, and segmented regression analysis.

Results Of the 56 patients, 38 had favorable outcomes ($mRS \leq 3$) and 18 had unfavorable outcomes ($mRS > 3$) at 3 months. A threshold effect at 38.2 °C was observed between postoperative body temperature and clinical outcomes. The mean age was 56 years ($SD=9$) for the > 38.2 °C group and 58 years ($SD=8$) for the ≤ 38.2 °C group, with a similar proportion of male patients (63% vs. 69%, $P=0.635$). Patients with postoperative fever had larger hematoma volumes (65 vs. 56 mL; $P=0.008$). Other characteristics were similar between the groups. Postoperative fever (> 38.2 °C) was independently associated with a 4.99-fold increased risk of unfavorable outcomes (95% CI = [1.13 to 25.90]; $P=0.040$), which remained significant after excluding patients with postoperative complications (adjusted RR = 16.03, 95% CI = [1.69 to 417.24]; $P=0.033$). The association was consistent across subgroups with different Glasgow Coma Scale scores, hematoma volumes, and intraventricular extension. Postoperative fever was also associated with longer NSICU stays

[†]Shuang Liu, Yunjian Zhang and Shengyang Su contributed equally to this work.

*Correspondence:
Xiaobiao Zhang
xiaobiao_zhang@163.com

Full list of author information is available at the end of the article



© The Author(s) 2024. **Open Access** This article is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License, which permits any non-commercial use, sharing, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if you modified the licensed material. You do not have permission under this licence to share adapted material derived from this article or parts of it. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by-nc-nd/4.0/>.

(3.1 vs. 2.3 days; $P=0.023$), longer hospital stays (17.2 vs. 13.6 days; $P=0.010$), more residual hematoma, and greater edema volume. Different antipyretic therapies did not affect outcomes.

Conclusions This study identifies a temperature threshold (38.2 °C) associated with poor outcomes in SICH patients undergoing endoscopic surgery. Further research is needed to mitigate postoperative fever and improve patient outcomes.

Keywords Endoscopic surgery, Spontaneous intracerebral hemorrhage, Postoperative fever, Clinical outcomes, Antipyretic therapy

Background

Spontaneous intracerebral hemorrhage (SICH) is a severe form of stroke with high mortality and disability rates. The incidence of SICH increases with age, and the early mortality rates range from 30 to 40% [1–4]. The treatment options for SICH include medical management, craniotomy, and endoscopic surgery. Endoscopic surgery is a minimally invasive technique that removes the hematoma through a small cranial opening using a camera and surgical instruments. This technique offers several benefits, such as less trauma, less bleeding, and faster recovery [5, 6]. Some clinical trials have shown that endoscopic surgery may improve the outcomes of SICH patients [7–9], but the optimal way to improve the functional outcomes of this procedure is still under investigation.

Body temperature is closely associated with neurological outcome in stroke patients. Previous studies have shown that a higher body temperature is associated with worse outcomes in patients with ischemic stroke who undergo endovascular thrombectomy [10] or in SICH patients who experience early neurological deterioration [11]. The INTERACT-3 trial showed that a care bundle approach, which includes antipyretic treatment (target body temperature ≤ 37.5 °C), can significantly improve the functional outcome of patients with acute cerebral hemorrhage [12]. However, the relationship between elevated body temperature and prognosis in SICH patients undergoing endoscopic surgery remains unclear. Elevated body temperature may worsen neurological conditions, metabolic balance, and other aspects of patients [13], or it may be a natural response to surgical trauma [14, 15] or brain hematoma [16, 17]. Therefore, it is crucial to monitor and manage postoperative fever promptly and effectively.

Despite advancements in the management of SICH, the impact of postoperative fever on patient outcomes remains unclear. This study aims to fill this knowledge gap by investigating the association between postoperative fever and clinical outcomes in patients who underwent endoscopic surgery for supratentorial SICH. We hypothesize that a specific temperature threshold is associated with poor outcomes, and identifying this threshold can inform clinical practice and guide future research on temperature management strategies in neurocritical care. The insights from this study will help optimize treatment

and care strategies to improve the prognosis of SICH patients.

Methods

Study design

This study adheres to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for reporting observational studies [18]. A completed STROBE checklist is provided as an additional file (Table S1).

We conducted a retrospective study to investigate the association between postoperative fever and clinical outcomes in patients with SICH who underwent endoscopic surgery. The data were sourced from the neurosurgery department of the People's Hospital of Jinping Miao, Yao and Dai Autonomous County, covering the period from July 2022 to June 2023. Data analysis was performed in January 2024.

Inclusion and exclusion criteria

The inclusion criteria were: (1) age ≥ 18 years; (2) confirmed diagnosis of supratentorial SICH by computed tomography (CT) scans; (3) endoscopic surgical evacuation of hematoma within 48 h of symptom onset; and (4) availability of follow-up data at 3 months after surgery. We excluded patients with: (1) other intracranial lesions such as tumors, aneurysms, or arteriovenous malformations; (2) infection or systemic inflammatory diseases before surgery; or (3) premorbid wishes against active treatment or care.

In the hospital, the indications for endoscopic surgery for SICH included: (1) supratentorial hematoma volume ≥ 30 mL; (2) neurological deterioration despite medical management; (3) Glasgow Coma Scale (GCS) score > 5 ; and (4) absence of contraindications for surgery, such as severe comorbidities or poor baseline functional status.

Outcome measures

Primary and Secondary Outcomes.

The primary outcome was neurological status at 3 months post-surgery, assessed using the modified Rankin Scale (mRS) score [19, 20]. We defined a good outcome as an mRS score of 0–3 and a poor outcome as an mRS

score of 4–6. Secondary outcomes included length of neurosurgical intensive care unit (NSICU) stay, length of hospital stay, and postoperative complications. DVT (deep vein thrombosis), pneumonia, and epilepsy were selected as perioperative complications due to their significant clinical relevance and potential impact on patient outcomes. These complications are commonly encountered in neurosurgical practice and have been well-documented in the literature for their association with increased morbidity and mortality [21–24].

Data collection

We collected data on demographic characteristics, medical history, clinical presentation, laboratory tests, imaging findings, surgical details, and postoperative complications from medical records. Hematoma volume and edema volume were calculated using preoperative CT scans and those taken on the first day post-surgery, using the ABC/2 method [25]. The presence of intraventricular expansion and deep hematoma location was determined from preoperative CT scans. Hematoma subtypes were categorized as lobar if they involved the cortical/subcortical white matter of the cerebral lobes or as deep if they were confined to the internal capsule, basal ganglia, or thalamus. Neurological outcomes at 3 months post-surgery were assessed using the mRS score obtained through telephone interviews or face-to-face visits conducted by trained neurologists.

Temperature management

Axillary temperature was measured using a mercury thermometer at least four times daily or more often if needed, as recorded in the medical records. Patients with elevated body temperature within 24 h after surgery were not cooled, as fever therapy (antipyretic drugs or physical cooling) has no clear benefit for febrile adults [26]. Cooling was initiated after 24 h based on the fever severity, duration, and cause, and the availability and feasibility of alternative interventions. Antipyretic therapy included physical cooling (ice packs or cooling blankets), pharmacological treatment (acetaminophen or nonsteroidal anti-inflammatory drugs), or both, as decided by the treating physician. The type, duration, and frequency of antipyretic therapy were recorded for each patient.

Statistical analysis

An a priori sample size calculation was not performed for this study. However, we included all eligible patients during the study period to increase the statistical power and generalizability. Based on previous literature, patients with ICH of hypertensive etiologic origin who presented hyperthermia showed a 5.3-fold higher risk of a poor outcome at 3 months [26]. We estimated the effect size for the association between postoperative fever and clinical

outcomes in SICH patients undergoing endoscopic surgery. Using this estimate, we performed a post hoc sample size calculation to determine whether our study was sufficiently powered to detect an effect [27]. Assuming an odds ratio of 5.3 and a sample size of 56, the power of our study is approximately 90%.

Continuous variables were compared using t-tests or Kruskal-Wallis rank sum tests, depending on the data distribution. Categorical variables were compared using chi-square tests or Fisher's exact tests, as appropriate. To evaluate the association between the maximum temperature within the first 24 h post-surgery and clinical outcomes at 3 months, we used generalized additive models, adjusting for potential confounders associated with the mRS score. A nonlinear relationship was tested using a spline regression model. If a nonlinear relationship was detected, we applied segmented regression analysis (also known as piece-wise regression), fitting separate line segments to each interval. A log-likelihood ratio test was used to determine the presence of a threshold, comparing a model without segmentation to a segmented regression model. The inflection point connecting the segments was obtained using maximum likelihood estimation with a two-step recursive method. The Spearman rank correlation coefficient was used to evaluate the correlation between the maximum temperature within the first 24 h post-surgery and different inflammatory markers or surgery-related variables. We also evaluated the impact of fever and different antipyretic treatments on clinical outcomes, adjusting for other potential factors.

Statistical analyses were performed using R software (version 4.2.0, R Development Team, Vienna, Austria). The power calculation was performed using G*Power software (version 3.1.9.7, Universität Düsseldorf, Germany) by selecting "Z tests" and "Logistic regression" as the test family and statistical test, respectively, and inputting the relevant parameters. The significance level was set at 0.05.

Results

Participant characteristics and temperature threshold

A total of 69 patients underwent endoscopic surgery for SICH during the study period. Of these, 62 met the inclusion criteria, while 7 were excluded based on the exclusion criteria. Thus, 56 patients were included in the final analysis. Among these 56 patients, 38 (67.9%) had favorable outcomes ($mRS \leq 3$), and 18 (32.1%) had unfavorable outcomes ($mRS > 3$). Preoperative temperature did not differ significantly between the groups (37.2 vs. 37.3 °C; $P=0.820$). However, the maximum temperature within the first 24 h post-surgery was significantly higher in the group with unfavorable outcomes (38.1 vs. 38.9 °C; $P=0.001$, Table S2). A threshold effect at 38.2 °C was observed between postoperative body temperature

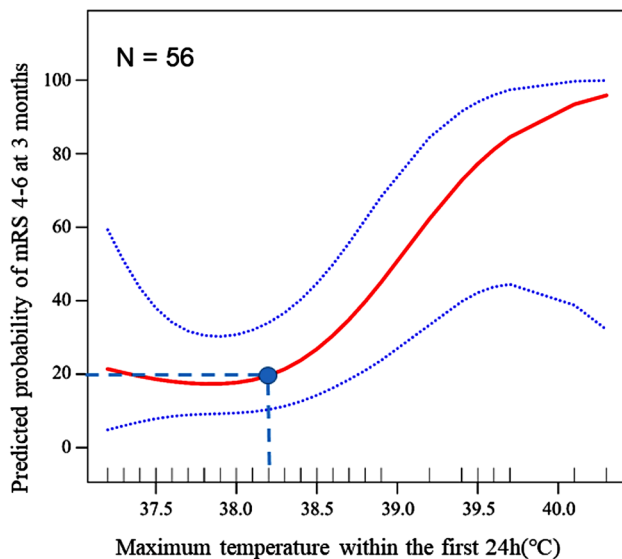


Fig. 1 Nonlinear association between maximum postoperative temperature and 3-month mRS score. This figure illustrates the nonlinear relationship between the maximum temperature recorded within the first 24 h post-surgery and the modified Rankin Scale (mRS) score at 3 months post-surgery. This relationship exhibits a threshold effect and persists even after adjusting for confounding factors such as age, time to hematoma evacuation, hematoma volume, GCS score, deep location, and intraventricular expansion

and clinical outcomes (Fig. 1). The risk of poor outcomes was not associated with maximum temperature until it exceeded 38.2 °C (RR=0.13, 95% CI = [0.02 to 0.86]; $P=0.215$). Beyond this threshold, the risk increased linearly with increasing maximum temperature (RR=40.24, 95% CI = [2.85 to 567.88]; $P=0.013$; Table S3)

Patients were divided into two groups based on this threshold: those with a maximum temperature exceeding 38.2 °C ($N=27$) and those with a maximum temperature of 38.2 °C or lower ($N=29$). Patients with postoperative fever exhibited significantly larger hematoma volumes compared to those without fever, with a mean difference of 9 mL (65 vs. 56 mL; $P=0.008$). The mean age was 56 years (SD=9) for the >38.2 °C group and 58 years (SD=8) for the ≤38.2 °C group, with a similar proportion of male patients in both groups (63% vs. 69%, $P=0.635$). Other characteristics, such as lifestyle factors, medical history, clinical presentation, surgical details, and GCS scores, were similar between the groups as described in detail in Table 1.

Primary outcome

Our multivariate analysis revealed that a maximum temperature exceeding 38.2 °C within the first 24 h post-surgery independently elevated the risk of a poor prognosis, with a relative risk (RR) of 4.99 (95% CI = [1.13 to 25.90]; $P=0.040$; Table 2). Importantly, this association persisted in a sensitivity analysis that excluded patients with

Table 1 Demographic and clinical characteristics grouped by postoperative temperature threshold of 38.2°C

Variables	> 38.2°C (N=27)	≤ 38.2°C (N=29)	P value
Age, y	56 (9)	58 (8)	0.237
Sex, male, %	17 (63.0)	20 (69.0)	0.635
Smoke, %	17 (63.0)	21 (72.4)	0.449
Hypertension, %	22 (81.5)	24 (82.8)	0.901
Drink, %	20 (74.1)	22 (75.9)	0.877
BMI	23.6 (2.5)	23.5 (2.6)	0.813
SBP, mmHg	203 (30)	199 (31)	0.632
Time to evacuation, h	14 (9–17)	10 (7–16)	0.183
NIHSS	10 (7–18)	10 (5–13)	0.378
Hematoma volume, mL	65 (57–72)	56 (46–64)	0.008*
Deep location, %	22 (81.5)	22 (75.9)	0.609
Intraventricular extension, %	18 (66.7)	16 (55.2)	0.379
Operative time, min	107 (32)	105 (26)	0.846
Blood loss, mL	114 (72)	104 (89)	0.636
Hematoma clearance > 90%, %	26 (96.3)	28 (96.6)	1.000
Temperature at admission(°C)	37.3 (0.4)	37.2 (0.4)	0.304
Surgical approach, %			0.660
Transylvian	20 (74.1)	23 (79.3)	
Transfrontal	4 (14.8)	2 (6.9)	
Transcortical	3 (11.1)	4 (13.8)	
GCS (6–14), %			0.258
6–8	11 (40.7)	6 (20.7)	
9–12	12 (48.1)	18 (62.1)	
13–14	3 (11.1)	5 (17.2)	

* Significant difference

Abbreviations: mRS: modified Rankin Scale; BMI: Body Mass Index; SBP: Systolic Blood Pressure; NIHSS: National Institute of Health stroke scale; GCS: Glasgow Coma Scale

Table 2 Multivariate regression analysis of the relationship between postoperative fever and mRS in different populations^a

	RR (95% CI)	P value
Cohort 1		
> 38.2°C vs. ≤ 38.2°C	4.99 (1.13, 25.90)	0.040*
Cohort 2		
> 38.2°C vs. ≤ 38.2°C	16.03 (1.69, 417.24)	0.033*

Abbreviations: mRS: modified Rankin Scale; RR: relative risk; CI: confidence interval

^a Adjusted for: age, hematoma volume, time to evacuation, deep location intraventricular expansion and GCS score

Cohort 1: all study population (N=56). Cohort 2: Patients with postoperative complications were excluded (N=36)

postoperative complications, further strengthening the link between early postoperative fever and adverse outcomes (RR=16.03; 95% CI = [1.69 to 417.24]; $P=0.033$).

The trend of increased risk with higher postoperative temperatures was observed across various subgroups, including those with dichotomized GCS scores, where the RR was 12.3 versus 4.0, though the interaction was not significant ($P=0.683$). Similarly, the presence or absence of intraventricular expansion did not significantly alter the RR (6.8 vs. 6.0; P for interaction=0.933),

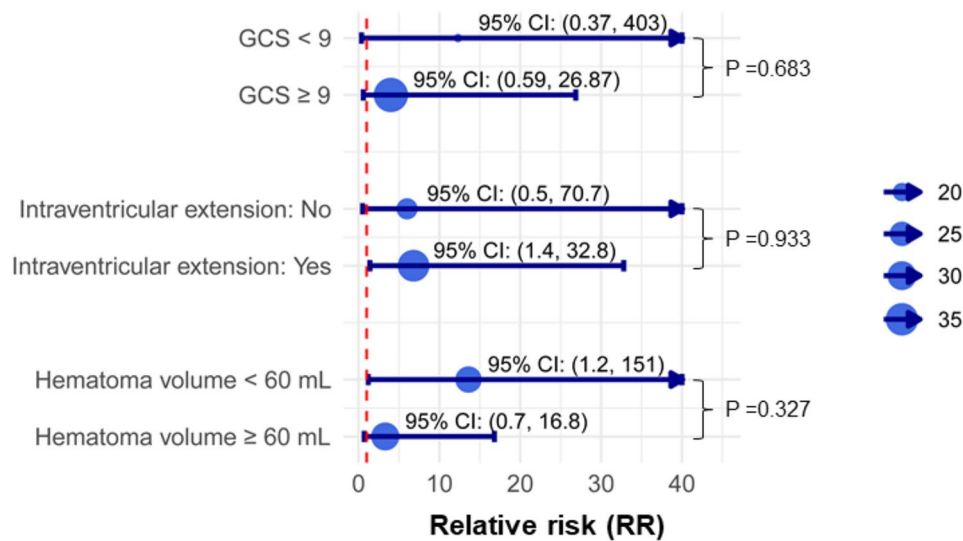


Fig. 2 Consistent Association between Postoperative Fever and 3-month mRS Score Across Subgroups. This figure demonstrates the consistent association between postoperative fever, defined as a body temperature exceeding 38.2 °C, and poor outcomes as measured by the modified Rankin Scale (mRS) at 3 months post-surgery. This association was observed across various subgroups, including those with dichotomized GCS score (RR=12.3 vs. 4.0; P for interaction=0.683), with or without intraventricular expansion (RR=6.8 vs. 6.0; P for interaction=0.933) and those different initial hemorrhage volumes (RR=13.6 vs. 3.3; P for interaction=0.327)

Table 3 Secondary outcomes comparison between fever and non-fever groups using a temperature threshold of 38.2 °C

Variables	≤ 38.2 °C (N=27)	> 38.2 °C (N=29)	P value
NSICU stays, d	2.3 (1.3)	3.1 (1.3)	0.023*
Hospital stays, d	13.6 (5.0)	17.2 (4.8)	0.010*
Complication, (%)			
Pneumonia	10 (34.5)	8 (29.6)	0.698
Epilepsy	2 (6.9)	1 (3.7)	0.596
DVT	3 (10.3)	2 (7.4)	1.000

* Significant difference

Abbreviations: NSICU: neurosurgical intensive care unit; DVT: deep vein thrombosis

nor did differences in initial hemorrhage volumes (RR=13.6 vs. 3.3; P for interaction=0.327; Fig. 2).

Secondary outcomes

Patients with temperatures above 38.2 °C had longer NSICU stays (3.1 vs. 2.3 days, $P=0.023$) and hospital stays (17.2 vs. 13.6 days; Table 3) than those with lower temperatures. We observed no significant differences in the rates of perioperative pneumonia (34.5% vs. 29.6%; $P=0.698$), epilepsy (6.9% vs. 3.7%; $P=0.596$), or DVT (10.3% vs. 7.4%; $P=1.000$) between the groups.

Factors associated with fever and effects of antipyretic therapy

No significant correlation was found between fever severity and leukocyte count ($\rho=0.079$, $P=0.562$), C-reactive protein level ($\rho=0.088$, $P=0.520$), procalcitonin level ($\rho = -0.013$, $P=0.926$), or operative time ($\rho=0.010$, $P=0.943$; Fig. S1). However, we observed

a significant positive correlation between maximum temperature within the first 24 h and edema volume ($\rho=0.615$, $P<0.001$) or residual hematoma ($\rho=0.580$, $P<0.001$; Fig. 3).

Among patients receiving antipyretic therapy, we found no significant impact of different antipyretic treatments on clinical outcomes after adjusting for maximum body temperature within the first 24 h postoperatively or other potential factors that may influence clinical outcomes (all $P>0.05$; Table 4).

Discussion

Our study demonstrates a significant association between postoperative fever and the prognosis of patients with SICH undergoing endoscopic surgery. Specifically, we found that a maximum temperature exceeding 38.2 °C within the first 24 h post-surgery is strongly linked to unfavorable outcomes at 3 months. Furthermore, patients with postoperative fever experienced longer stays in the NSICU and hospital, as well as greater residual hematoma and edema volumes. Notably, despite these associations, our findings indicate that antipyretic therapy had no significant impact on clinical outcomes, suggesting that its benefits may not be universal in this patient population. Taken together, these results imply that postoperative fever may serve as an indicator of the severity of brain injury, highlighting the importance of meticulous postoperative temperature monitoring and management. In this context, aggressive hematoma removal or the use of osmotic diuretics may be considered to improve patient outcomes.

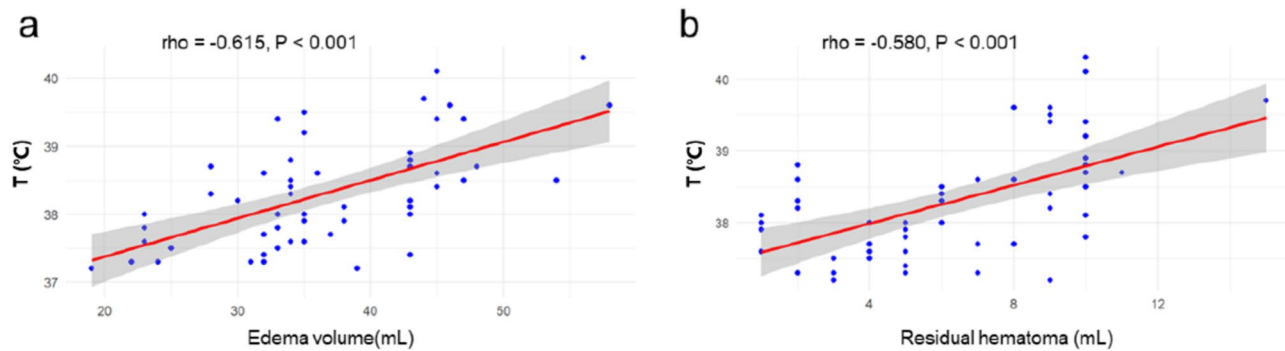


Fig. 3 Correlation between the Maximum Postoperative Temperature and Edema Volume and Residual Hematoma. The maximum temperature significantly correlates with edema volume (a) and residual hematoma (b)

Table 4 Association between Antipyretic Treatments and 3-Month post-surgery mRS score in different models among 29 patients

Antipyretic treatments	Model I β (95% CI) P	Model II β (95% CI) P
Without antipyretic treatment	1.0	1.0
Perfrigeration	1.8 (0.3, 11.3) 0.530	1.9 (0.3, 13.0) 0.534
Drugs plus perfrigeration	2.2 (0.3, 15.1) 0.423	1.6 (0.2, 16.1) 0.695

Abbreviations: mRS: modified Rankin Scale; CI: confidence interval

Model I: adjust for maximum temperature within the first 24 h; Model II: adjust for age, time to evacuation, hematoma volume, deep location, intraventricular extension and maximum temperature within the first 24 h

Our work contributes to the existing literature by exploring the relationship between postoperative fever and clinical outcomes in SICH patients undergoing endoscopic surgery, a growing yet relatively underexplored segment. This distinguishes our study from prior research that has largely focused on conservatively managed patients [13, 26, 28, 29]. By utilizing generalized additive models, we captured the intricate and variable nature of the fever response, revealing a nonlinear association between fever and patient outcomes. Notably, we found that fever below 38.2 °C was not predictive of poor prognosis, contrasting with earlier studies that reported reduced recovery rates in stroke patients with temperatures between 37.5 °C and 38 °C [30–32]. This discrepancy underscores the delicate balance between the potential benefits and drawbacks of mild to moderate temperature elevations on brain function following endoscopic surgery for SICH. This also supports the view that optimal body and brain temperatures for neuroprotection may vary based on factors such as insult type, severity, patient characteristics, and concurrent treatments [33].

Another finding of this study was that postoperative fever was associated with longer NSICU and hospital stays. However, this association did not correlate with higher rates of specific perioperative complications such

as pneumonia, epilepsy, or DVT. Patients undergoing neurosurgery are predisposed to DVT due to prolonged immobility and a hypercoagulable state, while postoperative pneumonia and seizures are common, particularly in patients with compromised consciousness or pre-existing brain pathologies. While some studies have shown an association with higher rates of pneumonia [21], sepsis [22], and DVT [23] in febrile patients, others [34], including our study, have found no such association. These discrepancies may stem from variations in fever definition, fever timing, surgery type, and patient population. More importantly, this observation implies that postoperative fever may serve as a surrogate marker for the severity of surgical stress and the patient's underlying condition, rather than being a direct causative factor for these complications. Prolonged NSICU and hospital stays can elevate the risk of nosocomial infections, adverse events, and healthcare costs, impacting the quality of care and resource utilization for patients with SICH undergoing endoscopic surgery. Given these potential consequences, it is crucial to explore the mechanisms linking postoperative fever to these outcomes and devise strategies to mitigate them.

Our study sheds valuable light on the complex phenomenon of postoperative fever in patients with SICH. Fever, a common clinical manifestation, can stem from various etiologies including infection, inflammation, tissue injury, or brain damage, as highlighted by Walter [35]. Notably, infection is typically not a factor within the first 48 h of surgery or NICU admission [36, 37]. This is underscored by our finding that postoperative fever within 24 h did not correlate with systemic inflammatory markers, suggesting a departure from the typical inflammatory response pathway. Furthermore, our sensitivity analysis reinforces the prognostic importance of postoperative fever, predicting poor outcomes even when infection-related complications are excluded. This implies that, in this context, fever may serve as a more reliable indicator of brain injury than inflammation. Intriguingly, we observed a positive association between

postoperative fever and residual hematoma and edema volumes, both of which are known to contribute to brain damage by modulating intracranial pressure and cerebral perfusion pressure. This observation underscores the need for future studies to explore the therapeutic potential of aggressive hematoma removal or the use of osmotic diuretics in mitigating postoperative fever and ultimately improving patient outcomes. Endoscopic surgery, a minimally invasive technique for hematoma evacuation, can still temporarily induce fever due to surgical trauma or hematoma removal [16]. Elevated body and/or brain temperature may exacerbate brain injury by altering brain physiology and increasing blood-brain barrier permeability. This could lead to more fluid and protein leakage and edema formation [26, 35]. While postoperative fever is associated with poor prognosis, it may also be a physiological response to surgery, hematoma, or tissue damage caused by residual hematoma and edema.

Our study found no correlation between antipyretic therapy and clinical outcomes in patients with postoperative fever, challenging the conventional use of antipyretic agents in neurocritically ill patients [38]. This suggests that antipyretic treatment may not be universally applicable to patients with postoperative fever, as it may not significantly impact outcomes. Additionally, antipyretics can cause side effects such as hypotension, hepatotoxicity, or bleeding [39]. Post-hematoma evacuation, a decrease in intracranial pressure and a modest increase in body temperature may enhance cerebral blood flow, tissue oxygenation, immune response, and neurogenesis, promoting brain recovery [40]. While severe traumatic brain injury patients with fever have shown worse outcomes [41] a systematic review found no effect of fever therapy on mortality or serious adverse events [42]. As previously mentioned, postoperative fever appears to be more closely associated with surgical trauma, stress, and edema from residual hematoma, rather than being a direct cause of poor outcomes. Hence, focusing solely on treating the manifestation of fever may not necessarily alter the ultimate clinical outcome. Our findings, though limited by the small sample size, suggest that the optimal temperature range for neuroprotection may vary from patient to patient and situation to situation. Therefore, antipyretic therapy should be individualized based on the patient's condition, the cause of fever, and the risk-benefit ratio of the treatment. Nevertheless, postoperative fever should not be neglected, as it may reflect the severity of surgical stress and the underlying condition of the patient, providing valuable information on the pathophysiology and prognosis of SICH.

This study had several strengths, such as the use of a well-defined population, a standardized surgical procedure, a rigorous outcome assessment, and a robust statistical analysis. However, it also has notable limitations.

The retrospective design and small sample size limit the generalizability of our findings. Additionally, this study was conducted at a single center, and there was a lack of data on the temporal changes in fever in homogeneous conservatively treated SICH patients for comparison, further limiting our conclusions. Therefore, our results should be interpreted with caution and validated by larger, prospective, multicenter studies.

Conclusions

This study provides valuable insights into the relationship between postoperative fever and clinical outcomes in SICH patients undergoing endoscopic surgery. By identifying a specific temperature threshold associated with poor outcomes, our findings contribute to the understanding of postoperative fever as a prognostic factor. Future research should focus on developing targeted interventions to mitigate postoperative fever and improve patient outcomes.

Abbreviations

SICH	Spontaneous intracerebral hemorrhage
mRS	Modified Rankin Scale
GCS	Glasgow Coma Scale
NSICU	Neurosurgical intensive care unit
DVT	Deep vein thrombosis
OR	Odds ratio
CI	Confidence interval

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12883-024-03898-4>.

Supplementary Material 1
Supplementary Material 2
Supplementary Material 3
Supplementary Material 4

Acknowledgements

We acknowledge the contributions of all the dedicated staff who participated in this study.

Author contributions

Shuang Liu, Yunjan Zhang and Xiaobiao Zhang contributed to the conception and design of the study. Shenyang Su, Jirao Ren, Jinyong Long, Shikui Cao and Fuhua Li contributed to the acquisition and analysis of the data. Shuang Liu, Zihui Gao and Qiangde Wang contributed to the clinical assessment of the data. The first draft of the manuscript was written by Shuang Liu and Yunjan Zhang. The final version of the manuscript was edited by Xiaobiao Zhang. All authors commented on previous versions of the manuscript. All authors reviewed the manuscript.

Funding

This work was supported by the "Science and Technology Innovation Action Plan" for Domestic S&T Cooperation [grant number 23015830700] from the Shanghai Municipal Science and Technology Commission and the Clinical Research Project [grant number 2023-LC-05] from the People's Hospital of Jinping Miao, Yao, and Dai Autonomous County.

Data availability

The author confirms that all data generated or analysed during this study are included in this published article.

Declarations

Ethics approval and consent to participate

This study followed the ethical standards of the institutional and national research committee and the 1964 Helsinki Declaration and its later amendments. The Ethics Committee of People's Hospital of Jinping Miao, Yao and Dai Autonomous County approved the study [grant number 2023-LL-0013]. We obtained written informed consent from all patients or their legal representatives before surgery and anonymized patient identities.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

¹Department of Neurosurgery, Zhongshan Hospital, Fudan University, 180 Fenglin Road, Shanghai 200032, China

²Department of Neurology, National Children's Medical Center, Children's Hospital of Fudan University, No. 399, Wanyuan Road, Shanghai 201102, China

³Department of Surgery, People's Hospital of Jinping Miao, Yao and Dai Autonomous County, No. 22, Guangjie Road, Honghe Prefecture, Yunnan Province 661599, China

⁴Department of Critical Care Medicine, People's Hospital of Jinping Miao, Yao and Dai Autonomous County, No. 22, Guangjie Road, Honghe Prefecture, Yunnan Province 661599, China

Received: 29 February 2024 / Accepted: 3 October 2024

Published online: 15 October 2024

References

- van Asch CJ, Luitse MJ, Rinkel GJ, van der Tweel I, Algra A, Klijn CJ. Incidence, case fatality, and functional outcome of intracerebral haemorrhage over time, according to age, sex, and ethnic origin: a systematic review and meta-analysis. *Lancet Neurol*. 2010;9(2):167–76. [https://doi.org/10.1016/S1474-4422\(09\)70340-0](https://doi.org/10.1016/S1474-4422(09)70340-0).
- Zahuranec DB, Lisabeth LD, Sánchez BN, Smith MA, Brown DL, Garcia NM, Skolarus LE, Meurer WJ, Burke JF, Adelman EE, Morgenstern LB. Intracerebral hemorrhage mortality is not changing despite declining incidence. *Neurology*. 2014;82(24):2180–6. <https://doi.org/10.1212/WNL.0000000000000519>.
- Greenberg SM, Ziai WC, Cordonnier C, Dowlatshahi D, Francis B, Goldstein JN, Hemphill JC, Johnson R, Keighner KM, Mack WJ, Mocco J, Newton EJ, Ruff IM, Sansing LH, Schulman S, Selim MH, Sheth KN, Sprigg N, Sunnerhagen KS. 2022 Guideline for the management of patients with spontaneous intracerebral hemorrhage: a Guideline from the American Heart Association/American Stroke Association. *Stroke*. 2022;53(7):e282–361. <https://doi.org/10.1161/STR.0000000000000407>.
- Jolink WM, Klijn CJ, Brouwers PJ, Kappelle LJ, Vaartjes I. Time trends in incidence, case fatality, and mortality of intracerebral hemorrhage. *Neurology*. 2015;85(15):1318–24. <https://doi.org/10.1212/WNL.0000000000002015>.
- Sun S, Li Y, Zhang H, Gao H, Zhou X, Xu Y, Yan K, Wang X. Neuroendoscopic surgery versus craniotomy for Supratentorial Hypertensive Intracerebral Hemorrhage: a systematic review and Meta-analysis. *World Neurosurg*. 2020;134:477–88. <https://doi.org/10.1016/j.wneu.2019.10.115>.
- Scaggiante J, Zhang X, Mocco J, Kellner CP. Minimally invasive surgery for Intracerebral Hemorrhage. *Stroke*. 2018;49(11):2612–20. <https://doi.org/10.1161/STROKEAHA.118.020688>.
- Guo W, Liu H, Tan Z, Zhang X, Gao J, Zhang L, Guo H, Bai H, Cui W, Liu X, Wu X, Luo J, Qu Y. Comparison of endoscopic evacuation, stereotactic aspiration, and craniotomy for treatment of basal ganglia hemorrhage. *J Neurointerv Surg*. 2020;12(1):55–61. <https://doi.org/10.1136/neurintsurg-2019-014962>.
- Fu C, Wang N, Chen B, Wang P, Chen H, Liu W, Liu L. Surgical Management of Moderate basal ganglia intracerebral hemorrhage: comparison of Safety and Efficacy of endoscopic surgery, minimally invasive puncture and drainage, and Craniotomy. *World Neurosurg*. 2019;122:e995–1001. <https://doi.org/10.1016/j.wneu.2018.10.192>.
- Noiphithak R, Yindeedeej V, Ratanavinitkul W, Duangprasert G, Nimmanitya P, Yodwisithsak P. Treatment outcomes between endoscopic surgery and conventional craniotomy for spontaneous supratentorial intracerebral hemorrhage: a randomized controlled trial. *Neurosurg Rev*. 2023;46(1):136. <https://doi.org/10.1007/s10143-023-02035-y>.
- Luo Y, Chen M, Fang J, Dong S, Ma M, Bao J, Feng L, He L. Relationship between body temperature and early neurological deterioration after Endovascular Thrombectomy for Acute ischemic stroke with large vessel occlusion. *Neurocrit Care*. 2022;37(2):399–409. <https://doi.org/10.1007/s12028-021-01416-9>.
- Leira R, Dávalos A, Silva Y, Gil-Peralta A, Tejada J, García M, Castillo J. Early neurologic deterioration in intracerebral hemorrhage. *Neurology*. 2004;63(3):461–7. <https://doi.org/10.1212/01.WNL.0000133204.81153.AC>.
- Ma L, Hu X, Song L, Chen X, Ouyang M, Billot L, et al. The third Intensive Care Bundle with blood pressure reduction in Acute Cerebral Haemorrhage Trial (INTERACT3): an international, stepped wedge cluster randomised controlled trial. *Lancet*. 2023;402(10395):27–40. [https://doi.org/10.1016/S0140-6736\(23\)00806-1](https://doi.org/10.1016/S0140-6736(23)00806-1).
- Honig A, Michael S, Eliahou R, Leker RR. Central fever in patients with spontaneous intracerebral hemorrhage: predicting factors and impact on outcome. *BMC Neurol*. 2015;15:6. <https://doi.org/10.1186/s12883-015-0258-8>.
- Erickson TC. Neurogenic Hyperthermia: a Clinical Syndrome and its Treatment. *Brain*. 1939;62(2):172–90. <https://doi.org/10.1093/brain/62.2.172>.
- Gillow SJ, Ouyang B, Lee VH, John S. Factors Associated with Fever in Intracerebral Hemorrhage. *J Stroke Cerebrovasc Dis*. 2017;26(6):1204–8. <https://doi.org/10.1016/j.jstrokecerebrovasdis.2017.01.007>.
- Kinoshita Y, Tominaga A, Saitoh T, Usui S, Takayasu T, Arita K, Sakoguchi T, Sugiyama K, Kurisu K. Postoperative fever specific to neuroendoscopic procedures. *Neurosurg Rev*. 2013. <https://doi.org/10.1007/s10143-013-0505-7>.
- Raviv N, Field N, Adamo MA. Postoperative fever workup in pediatric neurosurgery patients. *J Neurosurg Pediatr*. 2020;26(6):691–5. <https://doi.org/10.3171/2020.5.Peds2019>.
- von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The strengthening of reporting of observational studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *PLoS Med*. 2007;4(10):e296. <https://doi.org/10.1371/journal.pmed.0040296>.
- Yuan J, Wang Y, Hu W, Bruno A. The reliability and validity of a novel Chinese version simplified modified Rankin scale questionnaire (2011). *BMC Neurol*. 2020;20(1):127. <https://doi.org/10.1186/s12883-020-01708-1>.
- Saver JL, Chaisinanunkul N, Campbell BCV, Grotta JC, Hill MD, Khatri P, Landen J, Lansberg MG, Venkatasubramanian C, Albers GW. Standardized nomenclature for Modified Rankin Scale Global disability outcomes: Consensus recommendations from Stroke Therapy Academic Industry Roundtable XI. *Stroke*. 2021;52(9):3054–62. <https://doi.org/10.1161/STROKEAHA.121.034480>.
- Rincon F, Lyden P, Mayer SA. Relationship between temperature, hematoma growth, and functional outcome after intracerebral hemorrhage. *Neurocrit Care*. 2013;18(1):45–53. <https://doi.org/10.1007/s12028-012-9779-9>.
- Fordington S, Manford M. A review of seizures and epilepsy following traumatic brain injury. *J Neurol*. 2020;267(10):3105–11. <https://doi.org/10.1007/s00415-020-09926-w>.
- Barba R, Di Micco P, Blanco-Molina Á, Delgado C, Cisneros E, Villalta J, Morales MV, Bura-Riviere A, Debourdeau P, Monreal M. Fever and deep venous thrombosis. Findings from the RIETE registry. *J Thromb Thrombolysis*. 2011;32(3):288–92. <https://doi.org/10.1007/s11239-011-0604-7>.
- Liu S, Su S, Long J, Cao S, Ren J, Li F, Wang S, Niu H, Gao Z, Gao H, Wang D, Hu F, Zhang X. The impact of time to evacuation on outcomes in endoscopic surgery for supratentorial spontaneous intracerebral hemorrhage: a single-center retrospective study. *Neurosurg Rev*. 2023;47(1):2. <https://doi.org/10.1007/s10143-023-02237-4>.
- Sims JR, Gharai LR, Schaefer PW, Vangel M, Rosenthal ES, Lev MH, Schwamm LH. ABC/2 for rapid clinical estimate of infarct, perfusion, and mismatch volumes. *Neurology*. 2009;72(24):2104–10. <https://doi.org/10.1212/WNL.0b013e3181aa5329>.
- Iglesias-Rey R, Rodríguez-Yáñez M, Arias S, Santamaría M, Rodríguez-Castro E, López-Dequid I, Hervella P, Sobrino T, Campos F, Castillo J. Inflammation, edema and poor outcome are associated with hyperthermia in hypertensive intracerebral hemorrhages. *Eur J Neurol*. 2018;25(9):1161–8. <https://doi.org/10.1111/ene.13677>.

27. Faul F, Erdfelder E, Buchner A, Lang AG. Statistical power analyses using G*Power 3.1: tests for correlation and regression analyses. *Behav Res Methods*. 2009;41 4:1149–60. <https://doi.org/10.3758/brm.41.4.1149>.
28. Schwarz S, Häfner K, Aschoff A, Schwab S. Incidence and prognostic significance of fever following intracerebral hemorrhage. *Neurology*. 2000;54 2:354–61. <https://doi.org/10.1212/wnl.54.2.354>.
29. Bush RA, Beaumont JL, Liotta EM, Maas MB, Naidech AM. Fever burden and health-related quality of Life after Intracerebral Hemorrhage. *Neurocrit Care*. 2018;29 2:189–94. <https://doi.org/10.1007/s12028-018-0523-y>.
30. Hindfelt B. The prognostic significance of subfebrility and fever in ischaemic cerebral infarction. *Acta Neurol Scand*. 1976;53 1:72–9; <https://doi.org/10.1111/j.1600-0404.1976.tb04326.x>
31. Morimoto T, Ginsberg MD, Dietrich WD, Zhao W. Hyperthermia enhances spectrin breakdown in transient focal cerebral ischemia. *Brain Res*. 1997;746(1–2):43–51. [https://doi.org/10.1016/s0006-8993\(96\)01154-7](https://doi.org/10.1016/s0006-8993(96)01154-7).
32. Hervella P, Rodríguez-Yáñez M, Pumar JM, Ávila-Gómez P, Silva-Candal Ad, López-Loureiro I, Rodríguez-Maqueda E, Correa-Paz C, Castillo J, Sobrino T, Campos F, Iglesias-Rey R. Antihyperthermic treatment decreases perihematomal hypodensity. *Neurology*. 2020;94 16:e1738–48. <https://doi.org/10.1212/wnl.0000000000009288>.
33. Wang H, Wang B, Normoyle KP, Jackson K, Spitzer K, Sharrock MF, Miller CM, Best C, Llano D, Du R. Brain temperature and its fundamental properties: a review for clinical neuroscientists. *Front Neurosci*. 2014;8:307. <https://doi.org/10.3389/fnins.2014.00307>.
34. Narayan M, Medinilla SP. Fever in the postoperative patient. *Emerg Med Clin North Am*. 2013;31 4:1045–58. <https://doi.org/10.1016/j.emc.2013.07.011>.
35. Walter EJ, Hanna-Jumma S, Carraretto M, Forni L. The pathophysiological basis and consequences of fever. *Crit Care*. 2016;20 1:200. <https://doi.org/10.1186/s13054-016-1375-5>.
36. Blumstein GW, Andras LM, Seehausen DA, Harris L, Ross PA, Skaggs DL. Fever is common postoperatively following posterior spinal fusion: infection is an uncommon cause. *J Pediatr*. 2015;166 3:751–5. <https://doi.org/10.1016/j.jpeds.2014.11.033>.
37. Hocker SE, Tian L, Li G, Steckelberg JM, Mandrekar JN, Rabinstein AA. Indicators of central fever in the neurologic intensive care unit. *JAMA Neurol*. 2013;70 12:1499–504. <https://doi.org/10.1001/jamaneurol.2013.4354>.
38. Polderman KH. Induced hypothermia and fever control for prevention and treatment of neurological injuries. *Lancet*. 2008;371 9628:1955–69. [https://doi.org/10.1016/S0140-6736\(08\)60837-5](https://doi.org/10.1016/S0140-6736(08)60837-5).
39. Drewry AM, Ablordeppey EA, Murray ET, Stoll CRT, Izadi SR, Dalton CM, Hardi AC, Fowler SA, Fuller BM, Colditz GA. Antipyretic therapy in critically ill septic patients: a systematic review and Meta-analysis. *Crit Care Med*. 2017;45 5:806–13. <https://doi.org/10.1097/ccm.0000000000002285>.
40. Evans SS, Repasky EA, Fisher DT. Fever and the thermal regulation of immunity: the immune system feels the heat. *Nat Rev Immunol*. 2015;15 6:335–49. <https://doi.org/10.1038/nri3843>.
41. Diringner MN, Reaven NL, Funk SE, Uman GC. Elevated body temperature independently contributes to increased length of stay in neurologic intensive care unit patients. *Crit Care Med*. 2004;32 7:1489–95. <https://doi.org/10.1097/01.ccm.0000129484.61912.84>.
42. Holgersson J, Ceric A, Sethi N, Nielsen N, Jakobsen JC. Fever therapy in febrile adults: systematic review with meta-analyses and trial sequential analyses. *BMJ*. 2022;378:e069620. <https://doi.org/10.1136/bmj-2021-069620>.

Publisher's note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.