Elevated body temperature independently contributes to increased length of stay in neurologic intensive care unit patients*

Michael N. Diringer, MD, FCCM; Nancy L. Reaven, MA; Susan E. Funk, MBA; Gwen C. Uman, RN, PhD

Objective: Elevated temperature results in worse outcome in experimental models of cerebral ischemia and brain trauma. In critically ill neurologic and neurosurgical patients, elevated body temperature is common and is associated with neurologic deterioration and poor outcome. We sought to determine whether, after controlling for age, severity of illness, and complications, elevated body temperature remained an important predictor of intensive care unit (ICU) and hospital length of stay, mortality rate, and hospital disposition in a large cohort of patients emergently admitted to a neurologic ICU.

Design: Prospectively collected data (demographics, diagnosis, Acute Physiology and Chronic Health Evaluation II score, Glasgow Coma Scale score, daily maximum temperature, complications, disposition) were retrospectively reviewed.

Setting: A 20-bed neurology/neurosurgery ICU in a tertiary care academic, level I trauma, referral center.

Subjects: From 6,759 admissions, those admitted after an elective procedure with length of stay ≤1 day, those <18 yrs old, and those with incomplete data were excluded, leaving 4,295 patients for this analysis. First, a hierarchical multiple regression analysis was performed to determine whether elevated body temperature was an independent predictor of length of stay. Second, a path analysis was performed to define the relationships among elevated body temperature, complications, and length of stay. Finally, a matched, weighted sample was developed to quantify the difference in length of stay.

Interventions: None.

Measurements and Main Results: We measured ICU and hospital length of stay, mortality rate, and discharge disposition. The presence of elevated body temperature was associated with a dose-dependent longer ICU and hospital length of stay, higher mortality rate, and worse hospital disposition. The most important predictor of ICU length of stay was the number of complications ($\beta = .681$) followed by elevated body temperature ($\beta = .143$). In the matched, weighted population, the presence of elevated body temperature was associated with 3.2 additional ICU days and 4.3 additional hospital days.

Conclusion: In a large cohort of neurologic ICU patients, after we controlled for severity of illness, diagnosis, age, and complications, elevated body temperature was independently associated with a longer ICU and hospital length of stay, higher mortality rate, and worse outcome. (Crit Care Med 2004; 32:1489–1495)

KEY WORDS: temperature; intensive care; fever; length of stay; mortality; outcome

Elevated body temperature is common in critically ill patients with neurologic and neurosurgical disease. It is caused not only by infectious fever but also by endogenous pyrogens released by neuronal injury as well as the presence of blood in the cerebral parenchyma, ventricles, and subarachnoid space (1). In one study of neurologic intensive care unit (ICU) patients, body temperature exceeded 38.5°C in almost half, rising above that level an average of 4.7 times during their ICU stay (2). Elevated body temperature was more common in those with longer length of stay (LOS), and antipyretic therapy was often ineffective. In another study of patients hospitalized with acute brain insults, 83% of cardiac arrest patients, 70% of those with subarachnoid hemorrhage (SAH), and 68% of those with head injury developed fever (3).

Elevated brain temperature results in worse outcome in experimental models of cerebral ischemia and brain trauma. Increased levels of excitotoxins and oxygen radicals, destabilized cell membranes, and increased number of abnormal electrical depolarizations have been imputed in this process (4–8). Even a small increase in temperature of 0.5°C can produce a greater zone of injury and neuronal loss (8–11), and hyperthermia worsens injury even if it occurs 24 hrs after the original insult (12).

Several clinical studies have found that fever is an independent predictor of poor outcome following ischemic stroke (10, 13–15). Outcomes appear to be worse in febrile patients with intracerebral hemorrhage (16), SAH (2, 3, 17), and anoxic injury following cardiac arrest (18).

In the neurologic ICU population, as well as others, elevated body temperature may also increase ICU and hospital LOS. Addressing this question requires careful consideration of other factors that influence LOS, including severity of illness, age, and especially complications. In a small study of pediatric head injury patients, fever was found to be independently associated with longer ICU stays after controlling for injury severity and hypotension (19). The purpose of our study was to address this question in a much larger adult neurologic ICU population. We sought to determine whether, after controlling for other factors including age, severity of illness, and complications, fever remained an important factor in determining ICU and hospital LOS. We also explored the impact of elevated body

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From Neurology/Neurosurgery Intensive Care Unit (MND), Washington University, St. Louis, MO; Strategic Health Resources (NLR, SEF), La Canada, CA; and Vital Research (GCU), LLC, Los Angeles, CA.

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temperature on mortality rate and hospital disposition. To do so, we retrospectively reviewed clinical data on all admissions over 6 yrs to the 20-bed neurology/neurosurgery intensive care unit (NNICU) of a tertiary care academic referral center. In this article, the terms "fever" and "elevated temperature" are used interchangeably.

METHODS

Setting

The NNICU is a 20-bed ICU that provides all critical care services for patients admitted to the neurology and neurosurgery services. The hospital currently operates approximately 800 beds and is a level I trauma center. Care in the NNICU is provided concurrently by the primary service (neurology or neurosurgery) and the NNICU team. The team is made up of neurologic critical care attendings, neurologic ICU fellows, and dedicated residents and nurses who provide 24-hr per day coverage.

Data Collection

Information is recorded on all admissions to the NNICU using a computerized database (QuIC, Space Labs, Redmond, WA). Data collected include demographics, past medical history, clinical presentation, diagnoses, treatments, complications, and outcome. An individual nurse collects and records data using strict guidelines. The NNICU director performs periodic reviews to ensure data reliability. Patient data were retrospectively reviewed for this study. The data collection for the database and this specific analysis of those data were both approved by the Human Studies Committee of the Washington University School of Medicine.

The ICU attending's notes (the medical staff remained stable over the duration of the study period) were reviewed by an individual data coordinator to identify specific complications. Definitions of the major complications used by the ICU attendings were a) acute respiratory distress, a sustained compromise of pulmonary function resulting in a change in management; b) diarrhea, three or more loose stools/day; c) pneumonia, at least three of the following: fever, elevated white blood cell count, infiltrate on chest radiograph, positive sputum culture; d) urinary tract infection, positive urine culture with >100,000 colony counts; e) vasospasm, a focal or global neurologic deficit following aneurysmal SAH without other cause or angiographic evidence of focal vessel narrowing; f) increased intracranial pressure, a sustained intracranial pressure >20 mm Hg; and g) hyponatremia, serum sodium <135 mEq/L on two or more consecutive days.

Temperatures were recorded every 1 or 2 hrs on all patients in the NNICU and entered into a computerized charting system (Eclipsys, Eclipsys Corporation, Boca Raton, FL). Although the database did not record the site of temperature measurement, an audit of our current practice indicated that >90% temperatures are measured orally. Every 24 hrs the system automatically downloads the most extreme temperature to the ICU database. Thus, the database contained each patient's highest temperature during the previous 24-hr period. The medical director, attending staff, and type of resident coverage remained constant throughout the study period. There were no fever management protocol changes, and temperatures >38.5°C were routinely treated with acetaminophen.

A subset of variables was extracted from the database for this analysis and is presented in Table 1. The number of complications was calculated; to achieve a more normally distributed variable, those with four or more were grouped together. Other studies of fever in the ICU use the presence or absence of elevated temperature (19, 20) as the variable of interest. We chose to study not only the presence of elevated temperature but its degree by categorizing elevated temperature as low (37.5–38.4), moderate (38.5–39.0), and high (>39.0°C).

Study Population

Data collected on all admissions over a period of 6 yrs (January 1, 1996, to December 31, 2001) to a 20-bed neurology-neurosurgery ICU were analyzed for this study. From a total of 6,759 patients admitted during that period, data on patients under age 18 at the time of ICU admission (n = 49) and those with incomplete data (n = 731) were excluded, as were short-stay postprocedure patients, that is, those admitted for ≤1 day after elective surgery or interventional radiology (n = 1,684). For patients with multiple ICU admissions within a single hospital stay, only the longest ICU stay was included in the analysis. Following these exclusions, 4,295 patients were used for the study.

Statistical Analysis

Following univariate analyses, three statistical approaches were used. First, a hierarchical multiple regression analysis including all patients was performed to determine whether elevated body temperature was a significant independent predictor of LOS. Second, a path analysis was performed to further define the relationships among elevated body temperature, complications, and LOS. Finally, a matched, weighted sample was developed to allow quantification of the difference in LOS using Student's *t*-test (fever vs. no fever) and one-way analysis of variance with a Scheffé *post hoc* test (to compare four levels of fever).

Univariate analyses were used to compare the variables of interest between those who did and did not have elevated body temperature. Continuous variables were compared using independent Student's *t*-tests or Wilcoxon's rank sum test for variables that were not normally distributed. The chi-square statistic was used to compare categorical variables. Continuous variables are expressed as the mean ± SD and categorical variables as percentage of the group from which they were derived.

Regression Analysis

To determine whether elevated body temperature was independently associated with ICU and hospital LOS, a multiple linear regression model was developed to control for confounding variables. A hierarchical approach, with fever being inserted first and last, was used to enter variables into the regression model, to establish upper and lower bounds of the potential impact of elevated body temperature in explaining variance in ICU LOS. Values of $p < .10$ and $p < .05$ were used as limits for inclusion and removal of variables, respectively. All tests were two-tailed, and $p < 0.05$ was considered significant.

Path Analysis

To further explore the relationship among complications, fever, and LOS, a three-equation path analysis was performed. We sought to determine whether, after accounting for the influence of complications, elevated body temperature still had an impact on ICU LOS. Age and gender were not included in the analysis because they were earlier found not to influence LOS. The first equation computed coefficients for severity of illness (Acute Physiology and Chronic Health Evaluation [APACHE] II score) and the number of complications. The second equation treated elevated body temperature as the outcome variable, complications as the mediators, and severity as the exogenous variable. In the final equation, ICU LOS was the outcome variable, elevated body temperature and complications were mediators, and APACHE II was the exogenous variable.

Matched, Weighted Sample

A matched, weighted sample was developed to adjust for diagnosis, age, gender, severity of illness, and number of complications. We chose to perform this analysis in addition to the more traditional regression techniques because it creates results that have a meaningful interpretation at a practical level, such as the number of days difference in mean ICU length of stay be-

Table 1. Relationship between demographic and clinical variables, complications, and elevated body temperature

Fever Group	No Fever <37.5 °C (n = 1268)	Low 37.5–38.4 °C (n = 1591)	Medium 38.5–39.0 °C (n = 719)	High >39.0 °C (n = 717)
Age, mean ± SD[a]	58 ± 19.0	57.0 ± 18.8	57 ± 19.4	53 ± 18.8
Male gender, %[b]	51	50	51	57
APACHE II score, mean ± SD[c]	10.9 ± 7.0	12.1 ± 7.0	15.8 ± 7.6	18.3 ± 7.8
GCS, mean ± SD[d]	13.3 ± 3.1	12.5 ± 3.4	10.3 ± 4.1	9.0 ± 4.3
Diagnosis, %[b]				
AVM and elective aneurysm repair	4.3	4.7	2.5	1.1
Brain tumor	6.7	9.7	4.0	3.1
Cardiovascular/pulmonary	9.9	8.4	7.5	5.2
Intracerebral hemorrhage	17.0	15.1	20.9	21.1
Ischemic stroke	16.6	11.3	13.1	8.4
Other	6.9	7.6	7.2	10.0
Seizure	6.5	9.2	10.6	7.5
Spine disease	5.4	6.3	4.2	5.2
Subarachnoid hemorrhage	6.5	7.8	11.7	19.4
Subdural hematoma	6.1	7.1	2.9	2.2
Traumatic brain injury	14.3	12.9	15.4	16.9
Discharge disposition[b]				
Home	59	49	24	17
Rehabilitation facility	23	32	44	36
Nursing home	6	8	11	11
Mortality, %[d]	9.1	7.8	16.3	28.7
ICU LOS, mean ± SD[c]	1.7 ± 1.7	3.6 ± 4.0	7.4 ± 7.1	11.9 ± 9.2
Hospital LOS, mean ± SD[c]	7.6 ± 13.8	10.0 ± 9.1	15.3 ± 13.0	20.7 ± 17.2
No. complications/patient, mean ± SD	0.16 ± 0.5	0.4 ± 0.8	1.1 ± 1.3	1.8 ± 1.5
Complications, % of patients				
Acute respiratory distress	9	12	23	26
Diarrhea	6	5	12	19
Pneumonia	4	5	10	15
Urinary tract infection	9	11	16	18
Vasospasm	1	2	4	4
Increased ICP	2	2	4	9
Hyponatremia	1	2	4	7
Other	3	8	21	34

APACHE, Acute Physiology and Chronic Health Evaluation; GCS, Glasgow Coma Scale; AVM, arteriovenous malformation; ICP, intracranial pressure.
[a]High-temperature group is significantly different from all other groups ($p < .001$); [b]There was a significant association between level and gender, discharge disposition, and diagnosis ($p \leq .01$). Discharge disposition is shown as a percent of patients for whom this data element was known ($n = 4032$); totals do not sum to 100% because hospital transfers are not shown and mortality is shown separately as a percentage of the entire population ($n = 4295$); [c]no- and low-fever groups significantly lower than the two higher levels ($p < .001$); [d]levels are significantly different from one another ($p < .001$).

tween comparable patient populations with and without elevated body temperature.

We classified each of the 4,295 eligible discharges according to diagnosis, gender, age, APACHE II score on ICU admission, number of complications, and presence or absence of elevated body temperature (>38.0°C). The categories used for each variable are listed in Table 1. Each diagnosis/gender/severity/age category was matched by temperature status, so that a record was considered matched if a least one record with the opposite temperature status was present with the same diagnosis group, gender, severity class, and age group. For approximately 23% of patients, no such match was present in the study population. They were excluded, leaving 3,319 patients for the analysis.

To equalize the patient mix, we weighted records with matches in the data set to equalize the distribution by age, diagnosis, severity, and number of complications within the populations with and without elevated body temperature. This allowed for meaningful comparisons within the population as a whole as well as within individual diagnoses and by temperature level.

RESULTS

Population

The population included in the analysis consisted of 4,295 patients. Their characteristics are presented in Table 1. Univariate analyses indicated that the presence of elevated body temperature was associated with a longer ICU and hospital LOS, higher mortality rate, and worse hospital disposition (Table 1). The impact of fever varied considerably across diagnoses (Table 2).

Regression Analysis

The final regression models are presented in Tables 3 and 4. The most important predictor of ICU LOS was the complications score ($\beta = .681$) followed by elevated body temperature ($\beta = .143$), which accounted for between 2% and 11% of the variance in ICU LOS ($R^2 = 2–11$). This range was established by putting fever in first or last in the sequence of variables, since results in a regression analysis are affected by the order in which the variables are entered. Notably, the magnitude of the fever regression slope was substantially higher than that for severity of illness determined by the APACHE II score, as an explanation of ICU LOS. Age was inversely associated with LOS.

In predicting LOS of the entire hospital stay, the number of complications was the most important predictive factor but with much less power than when predicting ICU LOS. Fever was again the second

Table 2. Mortality rate and length of stay by diagnosis and temperature level

Diagnosis	None	Low	Medium	High	Total
Mortality rate (%) by temperature group					
A-V malformations	3.7	4.1	0.0	0.0	3.2
Brain tumor	1.2	0.6	3.4	22.7	2.8
Cardiovascular/pulmonary	3.2	8.3	18.5	16.2	8.9
Intracerebral hemorrhage	20.4	17.1	24.0	49.0	25.8
Ischemic stroke	7.1	14.5	31.9	45.0	18.0
Other	8.0	6.6	7.7	20.8	10.2
Seizure	0.0	1.4	7.9	9.3	3.6
Spine disease	4.4	3.0	0.0	8.1	3.8
Subarachnoid hemorrhage	15.9	10.5	11.9	28.1	17.5
Subdural hematoma	6.5	5.3	23.8	43.8	10.1
Traumatic brain injury	11.6	4.9	13.5	20.7	11.5
Total	9.1	7.8	16.3	28.7	13.1
LOS (days) by temperature group					
A-V malformations	2.1	3.7	10.4	23.4	9.9
Brain tumor	2.1	3.4	6.1	11.3	5.7
Cardiovascular/pulmonary	2.0	5.4	10.9	10.3	7.2
Intracerebral hemorrhage	1.5	3.3	6.9	10.3	5.5
Ischemic stroke	1.6	3.2	6.0	10.2	5.2
Other	2.4	5.1	8.6	9.9	6.5
Seizure	1.3	2.7	5.2	8.0	4.3
Spine disease	1.9	3.2	7.8	17.9	7.7
Subarachnoid hemorrhage	1.8	6.2	12.5	16.1	9.1
Subdural hematoma	2.0	2.7	4.4	10.7	4.9
Traumatic brain injury	1.1	2.0	5.2	11.0	4.8
Total	1.7	3.6	7.4	11.9	5.1

A-V, arteriovenous; LOS, length of stay.

Table 3. Predictors of intensive care unit length of stay

Predictors	β^i	Lowest R^2, %	Highest R^2, %	*p* Value
APACHE	.063			
Complications	.681			
Age	−.040			
Gender	.004			
SAH	.096	49	59	.000
Intracerebral hemorrhage	−.020			
Trauma	−.066			
Ischemic stroke	−.021			
Elevated body temperature	.143	1.8	11	.000

APACHE, Acute Physiology and Chronic Health Evaluation; SAH, subarachnoid hemorrhage.

Table 4. Predictors of hospital length of stay

Predictors	β	Lowest R^2, %	Highest R^2, %	*p* Value
APACHE	.053			
Complications	.424			
Age	.001			
Gender	−.004			
SAH	−.028	19	22	.000
Intracerebral hemorrhage	−.083			
Trauma	−.106			
Ischemic stroke	−.033			
Elevated body temperature	.092	0.8	4	.000

APACHE, Acute Physiology and Chronic Health Evaluation; SAH, subarachnoid hemorrhage.

most significant predictor of hospital LOS and was twice as powerful as severity of illness.

Path Analysis

The path analysis (Fig. 1) was performed to further evaluate the relationship among complications, elevated body temperature, and ICU LOS. The first equation indicated that greater severity of illness was significantly associated with having complications, accounting for 10% of the variance in complications as a group, independent of its impact on elevated body temperature. The second equation indicated that the number of complications had direct effects on elevated body temperature. The final equation found that the direct effect of elevated body temperature on ICU length of stay, after controlling for severity and number of complications, was significant (path coefficient = .12).

Matched, Weighted Sample

Presence of Fever. In the matched, weighted study population, the presence of elevated body temperature was associated with 3.2 additional ICU days and 4.3 additional hospital days ($p <$. 001, Student's *t*-test for unequal variances). The difference in ICU LOS was positive and statistically significant ($p < .01$) in every diagnostic group for the presence or absence of elevated body temperature, as summarized in Table 5.

The additional ICU days associated with elevated body temperature ranged from a high of 7.4 days for SAH patients to a low of 1.2 days for patients with subdural hematomas. In a majority of the 11 diagnostic groups, the presence of elevated body temperature was associated with a statistically significant difference in hospital LOS as well. As a result of the matching and weighting process, there were no significant differences in age and illness severity by temperature group or between gender and temperature group.

The impact on ICU and hospital LOS increased with higher levels of temperature. Over the entire neurologic ICU study population, each fever level (none, low, medium, and high) was significantly different from each other fever level for both ICU and hospital LOS (Scheffé *post hoc* test $p < .001$). High fever was associated with an ICU stay that was 7.7 days longer than in patients with no fever, whereas a low fever was associated with 1.5 additional ICU days compared with the no-fever group, as shown in Table 6.

Impact of Elevated body Temperature on Mortality Rate and Disposition

In addition to its impact on ICU and hospital LOS, elevated body temperature was associated with a dose-dependent increase in mortality rate, as shown in Tables 1 and 2. Although mild elevations in body temperature had no impact, mortality rate almost doubled in those with moderate fever and tripled in those with the highest temperatures. Similarly, hospital disposition worsened as temperature rose. The percent discharged to home decreased with each increase in temperature level, decreasing from 59% in patients with no fever to 17% in those with high temperatures (Table 1).

DISCUSSION

There is growing evidence that elevated body temperature may be detrimental to patients with acute neurologic insults. Most of the work to date has focused on the relationship between elevated body temperature, mortality rate, and functional outcome. In this study we broaden our understanding of the impact of elevated body temperature in the neurologic ICU by reporting that in a very large cohort of patients, after controlling for diagnosis, severity of illness, age, and complications (a frequent cause of elevated body temperature), elevated body temperature is associated with increased ICU and hospital LOS in a dose-dependent manner. This retrospective study, however, did not address causality or whether controlling elevated body temperature improves outcome.

The relationship between elevated body temperature and LOS is complex. Elevated body temperature may be a cause (13, 21, 22) as well as a consequence of (9) severe neurologic insults. Complications have a great influence on LOS in this population (23), yet they often also cause elevated body temperature. Finally, elevated body temperature may exacerbate the impact of neurologic insults such as vasospasm (17) or elevated intracranial pressure (24). Therefore, we chose to address the question of the relationship between elevated body temperature and LOS using a variety of analytical approaches to ensure the veracity of our findings.

The impact of elevated body temperature on ICU LOS may be mediated, in part, by worsening cerebral injuries that occur due to ongoing insults, such as are common in SAH patients. Although not directly addressed by our study, this possibility is consistent with our finding of worse outcome in febrile patients. The analyses also indicate that elevated body temperature was associated with in-

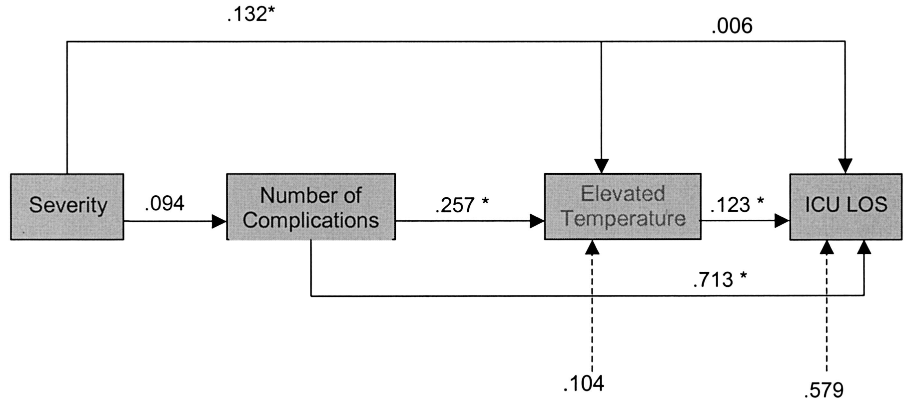

Figure 1. Path analysis of the relationship among complications, elevated body temperature, and length of stay (*LOS*). The first equation computed coefficients for severity of illness (Acute Physiology and Chronic Health Evaluation II score) and the number of complications. The second equation treated elevated body temperature as the outcome variable, complications as the mediators, and severity as the exogenous variable. In the final equation, intensive care unit (*ICU*) LOS was the outcome variable, elevated body temperature and complications were mediators, and Acute Physiology and Chronic Health Evaluation II was the exogenous variable. See text for interpretation. Values are R^2, $p < .001$.

Table 5. Difference in mean hospital and intensive care unit (ICU) length of stay (LOS) associated with elevated body temperature, by diagnosis in matched, weighted population ($n = 3319$)

Diagnosis	No. of Patients[a]	Difference in ICU LOS	Difference in Hospital LOS
Subarachnoid hemorrhage	298	7.4	9.7
Cardiovascular/pulmonary	263	4.0	6.0
Intracerebral hemorrhage	644	3.5	NS
Other	222	2.9	NS
Traumatic brain injury	505	2.8	5.2
Ischemic stroke	406	2.8	4.3
Spine disease	174	2.6	NS
A-V malformations + repairs	104	2.5	4.4
Seizure	297	2.3	4.6
Brain tumor	233	1.6	NS
Subdural hematoma	173	1.2	NS
Total Population	3,319	3.2	4.3

NS, no statistically significant difference at $p \leq .004$; A-V, arteriovenous.
[a]For ICU LOS; hospital LOS was available for 3,301 patients.

Table 6. Difference in mean hospital and intensive care unit (ICU) length of stay (LOS) compared with nonfever patients, by temperature level, in matched, weighted population ($n = 3,319$)

Temperature Level	No. of Patients	Difference in Hospital LOS	Difference in ICU LOS
High temperature	391	10.1	7.7
Medium temperature	479	6.1	4.2
Low temperature	1265	1.7	1.5

All differences are significant at $p \leq .001$. Each temperature level is significantly different from each other temperature level on both outcomes.

creased ICU LOS and worsened outcome in a dose-dependent manner. Low-grade temperature elevation was associated with a 1.5-day longer ICU stay, whereas the highest temperatures added 7.7 days. Similarly, mortality rate was three times higher in those with the highest temperatures, and discharge disposition suggested worse functional outcome.

Analysis of the matched, weighted sample found that the impact of elevated body temperature on LOS was considerable and varied across diagnostic groups. The impact of elevated body temperature on ICU LOS was significant in all diagnosis groups and highest in SAH, where the presence of elevated body temperature was associated with a 7.4-day increase in ICU length of stay. The relationship between elevated body temperature and hospital LOS was significant in all diagnosis groups except spine disease, brain tumors, and subdural hematomas. Hospital LOS had more variability, in part due to nonclinical factors, such as discharge planning concerns, that are likely to have more impact on LOS following discharge from the ICU. Furthermore, since for most diagnoses the increases in hospital LOS were greater than those for ICU LOS, we can conclude that the added ICU days associated with elevated body temperature did not generally replace non-ICU days but rather served to extend the patient's total hospital stay.

The path analysis used three steps to separate the effects of severity of illness, complications, and elevated body temperature on LOS. We found that patients with more severe illness were more likely to have a high number of complications and, in turn, those with complications were more likely to have elevated body temperature. Still, elevated body temperature had an independent effect on LOS that was of a similar magnitude as each complication and exceeded the impact of severity of illness. Of note, the predictive power of severity on ICU LOS was fully captured in its impact on the likelihood of complications and elevated body temperature; once complications and elevated body temperature were removed as factors, severity was statistically insignificant as a predictor of ICU LOS.

Still, the impact of elevated body temperature control remains unknown. Although a number of studies have addressed the use of therapeutic hypothermia, there has been no prospective study of an attempt to maintain euthermia in patients with acute brain insults. Thus it remains unproven as to whether control of elevated body temperature could improve outcome or decrease LOS. This is primarily a result of the lack of a means to easily and effectively maintain normal body temperature in this population. Acetaminophen and air cooling blankets effectively treat elevated body temperature in less than half of the patients (25). Prophylactic acetaminophen had minimal effect on body temperature in acute stroke patients (26, 27). Recently, new methodologies have been introduced that may be more effective in controlling elevated body temperature in these patients. Intravascular devices circulate cooled saline through balloons attached to a central venous catheter and appear to be effective in controlling established elevated body temperatures (28) and preventing them (29) without significant shivering. Improvements in surface cooling techniques have led to more effective devices (30, 31). Thus, it may now be feasible to determine whether more aggressive control of body temperature will improve outcome and reduce LOS.

The study has a number of strengths and limitations. Its primary strengths are the large number of patients included, the information about specific complications, and the veracity of the findings. Furthermore, the different analytical techniques employed all produced consistent results. Multiple regression revealed that elevated body temperature had a statistically significant impact on ICU LOS in this population. Path analysis confirmed that elevated body temperature, affected by severity and complications, was an important statistical predictor of ICU LOS. Analysis of the matched, weighted sample revealed that differences associated with elevated body temperature among comparable patient groups were large (3.2 days in the ICU on average), significant across multiple diagnoses, consistent in direction between ICU and hospital LOS, and increasingly large at progressively higher levels of body temperature.

The study's limitations include lack of more detailed data about use of antipyretics, other cooling methods, and antibiotics. Unfortunately, this information was not available from the database. A more precise measure of elevated body temperature (such are area under a temperature curve) would have been preferable. Additionally, the patients were stratified by the maximum temperature measurement recorded during the ICU stay, without regard to trends or duration. Yet, even with the less sensitive measure that we employed, we found a robust dose-dependent effect of temperature on outcome and LOS. It is important to note that there are other clinical and experimental conditions in which febrile temperatures may be beneficial due to their impact on immune function. Therefore, these result should not be generalized to other populations without further study.

In a large cohort of neurologic intensive care unit patients, after we controlled for severity of illness, diagnosis, age, and complications, we found that elevated body temperature was independently associated with a longer intensive care unit and hospital length of stay, higher mortality rate, and worse outcome.

CONCLUSION

In a large cohort of neurologic ICU patients, after we controlled for severity of illness, diagnosis, age, and complications, we found that elevated body temperature was independently associated with a longer ICU and hospital LOS, higher mortality rate, and worse outcome. It remains to be determined if control of elevated temperature can affect these relationships.

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