Intracranial and Blood Pressure Variability and Long-Term Outcome After Aneurysmal Subarachnoid Hemorrhage

By Catherine J. Kirkness, RN, PhD, Robert L. Burr, MSEE, PhD, and Pamela H. Mitchell, RN, PhD

**Background** Care of brain-injured patients in intensive care units has focused on maintaining arterial blood pressure and intracranial pressure within prescribed ranges. Research suggests, however, that the dynamic variability of these pressure signals provides additional information about physiological functioning and may reflect adaptive capacity.

**Objectives** To see if long-term outcomes can be predicted from variability of arterial blood pressure and intracranial pressure in patients with aneurysmal subarachnoid hemorrhage.

**Methods** Arterial blood pressure and intracranial pressure were monitored continuously for 4 days in 90 patients (74% women; mean age, 53 years) in an intensive care unit after subarachnoid hemorrhage. Variability of arterial blood pressure and intracranial pressure signals was calculated on 4 timescales: 24 hours, 1 hour, 5 minutes, and the difference of sequential 5-second means. The Extended Glasgow Outcome Scale was used to assess functional outcome 6 months after subarachnoid hemorrhage.

**Results** Pressure variability was better than mean pressure levels for predicting 6-month functional outcome. When initial neurological condition was controlled for, greater faster variability (particularly 5-second) was associated with better outcomes (typical $P<.001$), whereas greater 24-hour variability was associated with poorer outcomes (typical $P<.001$).

**Conclusions** The relationship between long-term functional outcome and variability of arterial blood pressure and intracranial pressure levels depends on the timescale at which the variability is measured. Because it is associated with better outcome, greater faster variability may reflect better physiological adaptive capacity. ([American Journal of Critical Care. 2009;18:241-251])
Research has began to show that greater physiological regularity and decreased physiological complexity are related to disease, aging, and mortality. Decreased physiological variability is thought to reflect uncoupling of system components normally involved in regulatory processes. The diminished communication between system components results in a decreased ability to respond appropriately to internal or external challenges to the system. In addition to the systemic integration of physiological system components involved in ABP and ICP regulation, cerebrovascular regulatory mechanisms normally respond to local changes in pressure in an attempt to ensure adequate cerebral perfusion. ICP variability may also reflect the specific responsiveness of these mechanisms.

Thus, consideration of the dynamic variability of ABP and ICP may provide additional information about physiological functioning, potentially reflecting dimensions of adaptive capacity. Such information could be clinically useful in determining which patients have a decreased capacity to respond to physiological perturbations, such as a decrease in ABP or oxygenation, and are at greater risk for adverse responses to nursing care, such as sustained increased ICP in response to positioning, that may contribute to secondary brain injury and poorer outcome. The purpose of this study was to examine the association between measures of the variability of ABP and ICP and outcomes in patients admitted to the intensive care unit (ICU) for management of SAH.

Methods

Design

This study was a descriptive correlational analysis of physiological data gathered as part of a randomized clinical trial to examine the effect of a highly visible display of cerebral perfusion pressure on management of that pressure and outcomes. The methods and results of the parent study are reported elsewhere.

Sample and Setting

The study was carried out at Harborview Medical Center in Seattle. The parent study included patients 16 years or older who had traumatic brain injury and cerebral aneurysms or arteriovenous malformations who were admitted to an ICU and underwent invasive ABP and ICP monitoring as part of the standard care. Of the 260 patients enrolled in the parent study, 90 had a diagnosis of aneurysmal SAH and were included in this analysis. Patients were enrolled during a 2-year period.

Measures

Demographic data and information on initial neurological condition (Glasgow Coma Scale [GCS] score), severity of SAH (Hunt and Hess score), diagnosis, management, and hospital course were recorded. The GCS is a widely used scale that allows level of consciousness to be quantified. Potential scores range from 3 (unresponsive) to 15 (alert and oriented). The Hunt and Hess score is determined on the basis of clinical neurological condition and

About the Authors

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reflects the severity of the SAH. Grades range from 1 (no symptoms or mild headache) to 5 (deep coma, moribund). Information on administration of major classes of medications that could affect ICP or ABP was recorded.

ABP measurements were obtained via intraarterial catheters connected to fluid-filled pressure transducers (Abbott Laboratories, Abbott Park, Illinois). ICP measurements were obtained via intraparenchymal Camino transducer-tipped catheters (Integra LifeSciences, Plainsboro, New Jersey). The ABP and ICP devices were connected to the bedside computer monitoring system (Spacelabs Medical, Redmond, Washington) and the signals were input from there to the study’s computer system. ABP and ICP data were saved as 5-second means.

Outcomes in the parent study were assessed 6 months after the SAH by trained interviewers who used the Extended Glasgow Outcome Scale (GOSE; scores: 1 = dead, 8 = upper part of good-recovery category). The GOSE was chosen in the parent study as a relevant measure of global functional outcome that could be used consistently across the subgroups of the study; thus, a stroke-specific outcome measure was not used. Outcome was dichotomized to (1) survival vs nonsurvival and (2) unfavorable (GOSE score, 1-4) vs favorable (GOSE score, 5-8).

ABP and ICP variability were calculated on 4 timescales: 5 seconds, 5 minutes, 1 hour, and 24 hours. On the 5-second timescale, variability was calculated as the root-mean-successive-square difference (RMSSD) of adjacent 5-second segments, reflecting the change from one 5-second average to the next. Variability on the other timescales was calculated as the standard deviation. The hourly standard deviation includes variability longer than 5 minutes up to 1 hour. The 24-hour standard deviation reflects variability longer than 1 hour up to 24 hours.

**Analysis**

Correlations between physiological variables and initial condition and medication use were examined by using Spearman correlation coefficients. The relationship between variability measures and outcomes was assessed by using binary logistic regression, with initial neurological condition (GCS score) controlled for.

**Results**

In keeping with the demographics of patients with SAH, the sample was predominantly women, with a mean age of 53 years (Table 1). Severity of the SAH was from mild to severe; most patients had mild to moderate SAH (Figure 1). The mean number of days from aneurysm rupture to initiation of study monitoring was 3.5 (SD, 3.3). Almost half (49%) had a ventriculostomy tube inserted for drainage of cerebrospinal fluid. Most patients underwent surgical clipping of their aneurysms (Table 1). A total of 19% underwent a craniectomy. Known preexisting conditions that could affect ABP included hypertension (54%), diabetes (5%), coronary artery disease (6%), and arrhythmias (6%). Survival was 80% at hospital discharge and 73% at 6 months after discharge. Six-month outcome by GOSE category is

**Table 1**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
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<td>Age, y Mean (SD)</td>
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<tr>
<td>Range</td>
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<tr>
<td>Female sex, % of patients</td>
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<tr>
<td>Score on Glasgow Coma Scale (GCS), mean (SD)</td>
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<tr>
<td>Range of GCS scores, % of patients</td>
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<tr>
<td>3-8</td>
<td>24</td>
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<tr>
<td>9-12</td>
<td>20</td>
</tr>
<tr>
<td>13-15</td>
<td>56</td>
</tr>
<tr>
<td>Aneurysm location, % of patients</td>
<td></td>
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<tr>
<td>Anterior circulation</td>
<td>82</td>
</tr>
<tr>
<td>Posterior circulation</td>
<td>18</td>
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<tr>
<td>Ventriculostomy, % of patients</td>
<td>49</td>
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<tr>
<td>Craniotomy, aneurysm clipping, % of patients</td>
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<tr>
<td>Coiling, % of patients</td>
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<tr>
<td>Craniectomy, % of patients</td>
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<tr>
<td>Vasospasm, % of patients</td>
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<td>Present</td>
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<tr>
<td>Severe</td>
<td>33</td>
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<td>Angioplasty, % of patients</td>
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<tr>
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<tr>
<td>Days in hospital Mean (SD)</td>
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<tr>
<td>Median</td>
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<td>Range</td>
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<tr>
<td>GCS score at discharge (survivors), mean (SD)</td>
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<tr>
<td>Range of GCS scores at discharge, % of survivors</td>
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<tr>
<td>3-8</td>
<td>1</td>
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<tr>
<td>9-12</td>
<td>17</td>
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<tr>
<td>13-15</td>
<td>82</td>
</tr>
<tr>
<td>Discharge disposition, % of patients</td>
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<td>Home</td>
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<td>Rehabilitation</td>
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<td>Skilled nursing facility</td>
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<tr>
<td>Other</td>
<td>6</td>
</tr>
<tr>
<td>Died</td>
<td>20</td>
</tr>
</tbody>
</table>
The median GOSE score of 5 reflects ability to function independently in the home but inability to return to previous work and considerable restrictions in social and leisure activities. The values of the physiological variables averaged over 4 days of monitoring are presented in Table 2. Both ICP and ABP variability increased as the timescale increased. None of the variability measures differed significantly according to whether the aneurysm was located in the anterior or posterior circulation. To assess whether variability differed depending on age, we examined the correlation between age and variability. Although age was not correlated significantly with any of the ICP variables, it was inversely correlated with mean ABP ($r = -0.22; P = .04$), ABP 5-second RMSSD ($r = -0.22; P = .04$), and 24-hour ABP standard deviation ($r = 0.40; P < .001$). As with age, the sex of the patient was not significantly associated with any of the ICP variables. However, women had greater 24-hour ABP variability than did men ($7.63 \text{ mm Hg vs } 6.34 \text{ mm Hg; } P = .04$).

Figures 3 and 4 present time-series plots of ICP and ABP for 24 hours that show variability on the different timescales. The $x$-axis represents time in hours and the $y$-axis represents pressure in millimeters of mercury. The top frame is the original time series of 5-second averaged data points. The subsequent frames break the variability into the different time components. The second frame shows variability that occurs over a period longer than 1 hour. The third frame shows variability that occurs over longer than 5 minutes but less than 1 hour. The bottom frame shows variability that occurs over longer than 5 seconds up to 5 minutes. Figure 3A shows high 5-second and 5-minute ICP variability in a patient who had a good 6-month outcome. Figure 3B shows low 5-second and 5-minute ICP variability in a patient who had an unfavorable outcome. Figure 4A illustrates high 5-second and 5-minute ABP variability (outcome was favorable), whereas Figure 4B shows low 5-second and 5-minute ABP variability (outcome was unfavorable).

The association between variability measures and SAH severity, as reflected by initial GCS score and Hunt and Hess score, is presented in Table 3. Greater faster variability (5-second RMSSD and 5-minute standard deviation) was significantly associated with better initial clinical condition (higher GCS score and lower Hunt and Hess score). This association was strongest in relation to ABP variability. The differences in variabilities are highlighted when groups with more severe SAH (Hunt and Hess score, 4 or 5) and less severe SAH (Hunt and Hess score, 1-3) are compared (Table 3). A significant positive association was found between ICP median level and all measures of ICP variability except 24-hour variability ($r = 0.24-0.29; P$ values, .02 to .006). Thus, ICP level was included as a control variable in the regression models. Because no similar association was found between ABP level and measures of ABP variability, ABP level was not included in the regression models.

The association between variability measures and cerebral vasospasm was examined. Vasospasm was categorized as present or absent and as severe, presented in Figure 2. The median GOSE score of 5 reflects ability to function independently in the home but inability to return to previous work and considerable restrictions in social and leisure activities.

The values of the physiological variables averaged over 4 days of monitoring are presented in Table 2. Both ICP and ABP variability increased as the timescale increased. None of the variability measures differed significantly according to whether the aneurysm was located in

ICP and ABP variability were better predictors of 6-month functional outcome than were mean pressure levels.
defined by transcranial Doppler criteria, or other. Although ICP level differed significantly between patients with vasospasm (mean, 12.6; SD, 7.4) and patients without vasospasm (mean, 7.3; SD, 4.3), after level was controlled for, none of the ICP variability measures differed significantly between the 2 groups. Neither ICP level nor ICP variability measures differed significantly between subgroups of patients with severe vasospasm and all other patients. ABP level and variability measures did not differ significantly between patients with and patients without vasospasm or between patients with severe vasospasm and other patients with vasospasm.

Figure 5 presents the odds ratios for 6-month survival by mean ICP level and by measures of variability, with the initial clinical condition (GCS score) controlled for (and additionally for the measures of variability, with ICP level controlled for). Although the association between mean ICP level and survival was not significant, ICP variability was a significant predictor of survival on the 5-second, 5-minute, and 24-hour timescales. Whereas greater faster (5-second or 5-minute) variability was associated with greater odds of being alive 6 months after discharge, greater slower (24-hour) variability was associated with lower odds of 6-month survival.

The pattern of greater 5-second or 5-minute variability and better odds of survival was also present in relation to ABP (Figure 6). As with 24-hour ICP variability, greater 24-hour ABP variability was associated with significantly lower odds of 6-month survival.

To examine further whether the association between ABP and ICP variability and outcome is predictive not only of survival but also of functional ability at 6 months, we repeated the preceding analyses, dichotomizing 6-month outcome to favorable (GOSE score, >4) and unfavorable (GOSE score, ≤4). As with survival, median ICP level was not significantly associated with functional outcome (Figure 7). ICP variability on both the 5-second and 5-minute timescales was significantly associated with greater odds of favorable outcome at 6 months. Although the relationship between 24-hour ICP variability and favorable outcome was in the same direction as that of 24-hour variability and survival, it showed only a strong trend and was not statistically significant.

ABP level was not a significant predictor of 6-month survival; however, higher ABP level over 4 days of monitoring was associated with significantly lower odds of favorable outcome at 6 months (Figure 8). Greater 5-second RMSSD variability in ABP was associated with significantly greater odds of favorable outcome. Conversely, greater 24-hour variability in ABP was associated with significantly lower odds of favorable outcome.

The percentage of patients receiving major classes of medication with potential effects on ABP or ICP is presented in Table 4. All patients received calcium channel blockers as the standard of care for management of SAH. In addition, all patients received analgesics during the period of monitoring, and most received anxiolytics/sedatives/hypnotics. Because of the highly variable amounts of as-needed medications administered, the median number of doses (based on standard mean doses) received during the 4 days of monitoring was calculated for analgesics (median, 11.0; range, 1-76), anxiolytics/sedatives/hypnotics (median, 1.8; range, 0-466), and diuretics (median, 0.9; range, 0-38). The high end of the range of anxiolytics/sedatives/hypnotics was related to administration of high-dose propofol to several patients.

Median ICP was significantly correlated with the number of doses of analgesics (r = 0.28; P = .008) and diuretics (r = .29; P = .005). No significant correlations were found between ICP 5-second RMSSD and 5-minute standard deviation and any of the major classes of medications. ICP hourly standard deviation was significantly correlated with anxiolytic/sedative/hypnotic dose (r = .31; P = .003) and diuretic dose (r = 0.21; P = .04). Daily ICP standard deviation was also significantly correlated with diuretic dose (r = 0.28; P = .008).

### Table 2

<table>
<thead>
<tr>
<th>Variability measure</th>
<th>Arterial blood pressure, mm Hg</th>
<th>Intracranial pressure, mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Range</td>
<td>103.2 (10.7)</td>
<td>11.6 (7.3)</td>
</tr>
<tr>
<td></td>
<td>76.8-131.4</td>
<td>-1.7 to 42.2</td>
</tr>
<tr>
<td>5-second RMSSD</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td></td>
<td>3.5 (1.5)</td>
<td>1.2 (0.87)</td>
</tr>
<tr>
<td></td>
<td>1.6-10.1</td>
<td>0.4-6.1</td>
</tr>
<tr>
<td>Standard deviation</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>5-minute</td>
<td>3.7 (1.1)</td>
<td>1.6 (0.9)</td>
</tr>
<tr>
<td></td>
<td>1.6-7.9</td>
<td>0.5-5.3</td>
</tr>
<tr>
<td>5-minute to 1-hour</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td></td>
<td>3.9 (1.1)</td>
<td>1.7 (0.7)</td>
</tr>
<tr>
<td></td>
<td>2.3-8.6</td>
<td>0.7-4.2</td>
</tr>
<tr>
<td>1-hour to 24-hour</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td></td>
<td>7.3 (2.6)</td>
<td>3.6 (1.7)</td>
</tr>
<tr>
<td></td>
<td>2.7-21.3</td>
<td>0.5-8.3</td>
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</tbody>
</table>

Abbreviation: RMSSD, root-mean-successive-square difference.

**Variability outside the normal range likely reflects ineffective adaptive mechanisms.**
Median ABP was significantly correlated with anxiolytic/sedative/hypnotic dose ($r = 0.25; P = .02$) and corticosteroid dose ($r = 0.39; P < .001$). ABP 5-second RMSSD was significantly correlated with antiarrhythmic (yes/no) ($r = -0.22; P = .03$), diuretic dose ($r = -0.23; P = .03$), and vasodilator dose ($r = 0.24; P = .02$). The 5-minute ABP standard deviation was not significantly correlated with any of the major drugs classes. Hourly

Figure 3 Variability in intracranial pressure (ICP) over 24 hours on 4 time scales: top panel, original time series of 5-second data points; second panel, hourly variability; third panel, 5-minute variability; bottom panel, 5-second variability. A, High variability; favorable outcome (score on Extended Glasgow Outcome Scale, 5). B, Low variability; unfavorable outcome (score on Extended Glasgow Outcome Scale, 1).
ABP standard deviation was significantly correlated with anxiolytic/sedative/hypnotic dose ($r = 0.38; P < .001$), diuretic dose ($r = 0.22; P = .04$), and vasodilator dose ($r = 0.22; P = .04$). The 24-hour ABP variability was significantly correlated with administration of adrenergic blockers ($r = 0.21; P = .049$), administration of antiarrhythmic agents ($r = 0.23; P = .03$), and anxiolytic/sedative/hypnotic dose ($r = 0.22; P = .04$).

**Figure 4** Variability in arterial blood pressure (ABP) over 24 hours on 4 time scales: top panel, original time series of 5-second data points; second panel, hourly variability; third panel, 5-minute variability; bottom panel, 5-second variability. A, High ABP 5-second root-mean-successive-square distance (RMSSD), 5-second standard deviation variability; favorable outcome (score on Extended Glasgow Outcome Scale, 5). B, Low ABP 5-second RMSSD, 5-minute standard deviation; unfavorable outcome (score on Extended Glasgow Outcome Scale, 1).
Although adaptive mechanisms normally maintain physiological variables within ranges compatible with maintenance of system integrity and functioning, these measures are not static and variability is a feature of healthy systems. Variability outside the normal healthy range in either direction, however, is likely to reflect ineffective adaptive mechanisms in disease or injury. ABP and ICP variability after SAH may provide clinically important information about physiological responsiveness of the cardiovascular and cerebrovascular systems that reflects impaired functioning. Patients with impaired physiological responsiveness, as reflected by abnormal variability, could be at high risk for further physiological derangement.

In addition to functioning of intrinsic adaptive mechanisms, external factors such as environmental influences and medical and nursing interventions contribute to physiological variability. The degree to which these factors positively or negatively affect variability, however, is not well documented. In this study, we measured the overall variability of ICP related to all factors soon after SAH. The independent contributions of disease severity and administration of medications were examined.

ABP variability can be related to both physiological and pathophysiological factors and has been examined as an indicator of cardiovascular control and for its potential prognostic significance. Overall ABP variability is due to several different factors that act on different timescales, from seconds to days. This variability includes fluctuations related to intrinsic cardiovascular regulation, activity, and a 24-hour circadian variability. In addition, disease and pharmacological agents influence ABP variability.

ABP variability has been examined in relation to hypertension and cardiovascular and cerebrovascular risk. Higher measures of ABP variability are associated with carotid artery damage, increased cardiovascular mortality, cerebral white matter lesions, cardiac structure damage, stroke, and myocardial infarction, particularly in patients with hypertension. Our findings agree with a general hypothesis, which is supported by previous research, that greater ABP variability is associated with more severe disease manifestations. However, findings of greater ABP variability and more severe disease manifestations in critically ill patients with SAH have not previously been documented.

Little research has been done on simple indicators of ICP variability, such as standard deviation, in patients with acute SAH. In a study of 8 patients with various cerebrovascular disorders, ICP standard

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Correlations between severity of subarachnoid hemorrhage and variability measures</th>
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<tbody>
<tr>
<td>Variability measure</td>
<td>GCS score</td>
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<tr>
<td>ABP RMSSD</td>
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<tr>
<td>ABP 5-minute standard deviation</td>
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<td>ICP RMSSD</td>
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<td>ICP 5-minute standard deviation</td>
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<table>
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<tr>
<th>Variability measure</th>
<th>Hunt and Hess score</th>
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<td>ICP 5-minute standard deviation, mm Hg</td>
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</table>

Abbreviations: ABP, arterial blood pressure; GCS, Glasgow Coma Scale; ICP, intracranial pressure; RMSSD, root-mean-successive-square difference.

Figure 5 Odds ratios for 6-month survival by mean intracranial pressure (ICP) level and by measures of variability, with the initial clinical condition (score on Glasgow Coma Scale) controlled for (and additionally for the measures of variability, with ICP level controlled for).

Abbreviations: CI, confidence interval; RMSSD, root-mean-successive-square difference; SD, standard deviation.
deviation was evaluated for 4 minutes. ICP standard deviation was elevated (6-10 mm Hg), particularly during periods of decompensation, except in the course of cerebral vasospasm, when it was low. In our study, ICP variability was not significantly associated with cerebral vasospasm. Although cerebral vasospasm decreases the amplitude of individual intracranial pressure waveforms, this effect may not be reflected in 5-second ICP standard deviation means.

ABP is the primary input for ICP. We found a significant positive association between ABP and ICP variability across subjects at the 5-second ($r = 0.50; P < .001$), 5-minute ($r = 0.33; P = .001$), and 24-hour ($r = 0.32; P = .002$) timescales. However, this association does not address the within-subject impact of ABP variability on ICP variability. ICP variability is affected by numerous factors other than ABP level, including the degree of transmission of ABP to ICP, venous drainage from the head, cerebrospinal fluid circulation, and cerebral autoregulation. Cerebral autoregulation is a mechanism whereby cerebral blood vessels constrict or dilate in response to changes in ABP to ensure a consistent blood flow to the brain. Changes in the diameter of cerebral blood vessels can lead to changes in blood volume, resulting in changes in ICP. Cerebral autoregulation is normally rapid; compensatory changes begin within seconds.

Variability of ICP and ABP soon after SAH is a significant predictor of 6-month outcome. However, the relationship between variability and outcome depends on the timescale over which variability is assessed. Although greater 5-second RMSSD and 5-minute standard deviation variability is associated with increased odds of both survival and good outcome, conversely, greater variability for timescales of 1 hour or longer is associated with decreased odds of survival and good outcome. Greater 5-second variability of both ICP and ABP was the strongest predictor of survival and good outcome; thus, this faster variability may reflect more effective functioning of adaptive mechanisms. Because of its significant association with poorer outcome, greater variability for time spans longer than 1 hour may reflect decreased integrated ability of adaptive mechanisms to respond to physiological alterations or challenges to the system. ABP and ICP variability was measured relatively soon after SAH. We do not know if this variability would change as recovery occurs or in the long term.

The minimum resolution of data points in our analysis is 5 seconds, so the function of mechanisms that effect especially rapid changes in ICP and ABP is not reflected. Such mechanisms include beat-by-beat fluctuations related to the cardiac cycle, most fluctuations in the respiratory cycle (for respiratory rates of 12/min or faster), and rapid autonomic nervous system modulation of ABP. The impact of sympathetic nervous system activity and Mayer waves would be compatible with fluctuations represented in the ABP 5-minute standard deviation. Further study of the effect of circulating catecholamines on ABP and ICP variability after SAH would be of interest. Other contributors

ICP variability was not associated with cerebral vasospasm.
to both ABP and ICP variability for timescales longer than 5 seconds include nursing care, environmental stimuli, and patients’ activity. Factors affecting longer-term ABP variability, for example, hourly, include functioning of longer-term feedback mechanisms such as the renin-angiotensin system.

When the association between administration of major groups of medications and ICP variability was examined, all significant correlations were in a positive direction. Administration of diuretics and antiarrhythmic medications was associated with less 5-second ABP variability. All other significant correlations between medications and ABP variability reflected greater variability with administration of medications. Although the administration of several of the medications could decrease ABP and ICP variability, such as sedation that decreases activity level, most medications were not associated with a decrease in variability. The medications may actually have little effect on variability or may increase variability, or the reason for which they are given may continue to have a greater effect on increasing variability than the medications’ effect to decrease variability. This relationship is also apparent in relation to level; for example, higher doses of analgesics and diuretics, both given to manage increased ICP, are associated with higher median ICP.

The observation of trends over periods longer than that routinely displayed on bedside clinical monitors is informative in relation to physiological state and prediction of outcome. Although calculation of the standard deviation of physiological measures such as ABP and ICP is simple and quantifies pressure variability, even visual records of trends over various periods provide meaningful qualitative information about variability on various timescales. The original ABP and ICP time series in the top frames of Figures 3 and 4 that display trends over 24 hours clearly show differences in variability on various timescales between those 2 patients.

Indices reflecting faster variability were positively associated with better long-term outcome. It is plausible that both faster and slower variability reflect physiological adaptive capacity. Our findings and those of other studies of a relationship between greater ABP variability over 24 hours and higher cerebrovascular and cardiovascular morbidity suggest that greater longer-term variability may reflect poorer functioning of adaptive mechanisms and decreased physiological regulatory capacity. In addition, the association in our study between greater faster variability and better outcome may suggest that faster physiological variability reflects a regulatory system capable of responding rapidly and more effectively to internal and external perturbations that occur in a critical care clinical situation. Thus, real-time visual assessment of pressure variability may be useful clinically to identify critically ill patients who have decreased physiological adaptive capacity and are therefore less likely to be able to compensate for both physiological and pathophysiological challenges. Nursing care for high-risk persons could then be specifically targeted to minimize such challenges. The development and testing of such interventions requires further study.

Further research is also needed to determine the most appropriate and meaningful measures to

![Figure 8](http://ajcc.aacnjournals.org/)
assess dynamic variability of physiological measures in the clinical setting and to understand better the relationship between physiological variability, adaptive capacity, and outcome. Whether nursing or medical intervention directed specifically at changing ABP or ICP variability can be effective, and whether this alteration is ultimately associated with changes in outcome, also remains to be studied.

Conclusion

Beyond ABP and ICP level, simple measures of variability of ABP and ICP provide prognostic information about 6-month survival and functional outcome.

The direction of the association depends on the timescale on which the variability is measured. Greater faster ABP and ICP variability as measured in this study in patients soon after SAH may reflect relatively fast cardiovascular and cerebrovascular physiological responsiveness and are associated with better outcomes. Conversely, greater slower ABP and ICP variability is associated with poorer outcome.

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