Hemoglobin Concentration and Cerebral Metabolism in Patients With Aneurysmal Subarachnoid Hemorrhage

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Background and Purpose—The optimal hemoglobin (Hgb) target after aneurysmal subarachnoid hemorrhage is not precisely known. We sought to examine the threshold of Hgb concentration associated with an increased risk of cerebral metabolic dysfunction in patients with poor-grade subarachnoid hemorrhage.

Methods—Twenty consecutive patients with poor-grade subarachnoid hemorrhage who underwent multimodality neuromonitoring (intracranial pressure, brain tissue oxygen tension, cerebral microdialysis) were studied prospectively. Brain tissue oxygen tension and extracellular lactate/pyruvate ratio were used as markers of cerebral metabolic dysfunction and the relationship between Hgb concentrations and the incidence of brain hypoxia (defined by a brain tissue oxygen tension <20 mm Hg) and cell energy dysfunction (defined by a lactate/pyruvate ratio >40) was analyzed.

Results—Compared with higher Hgb concentrations, a Hgb concentration <9 g/dL was associated with lower brain tissue oxygen tension (27.2 [interquartile range, 21.2 to 33.1] versus 19.9 [interquartile range, 7.1 to 33.1] mm Hg, \( P = 0.02 \)), higher lactate/pyruvate ratio (29 [interquartile range, 25 to 38] versus 36 [interquartile range, 26 to 59], \( P = 0.16 \)), and an increased incidence of brain hypoxia (21% versus 52%, \( P < 0.01 \)) and cell energy dysfunction (23% versus 43%, \( P = 0.03 \)). On multivariable analysis, a Hgb concentration <9 g/dL was associated with a higher risk of brain hypoxia (OR, 7.92; 95% CI, 2.32 to 27.09; \( P = 0.01 \)) and cell energy dysfunction (OR, 4.24; 95% CI, 1.33 to 13.55; \( P = 0.02 \)) after adjusting for cerebral perfusion pressure, central venous pressure, \( \text{PaO}_2/\text{FiO}_2 \) ratio, and symptomatic vasospasm.

Conclusions—A Hgb concentration <9 g/dL is associated with an increased incidence of brain hypoxia and cell energy dysfunction in patients with poor-grade subarachnoid hemorrhage. (Stroke. 2009;40:00-00.)

Key Words: brain oxygen ■ cerebral microdialysis ■ hemoglobin ■ subarachnoid hemorrhage

Experimental animal evidence demonstrates an association between anemia and reduced brain tissue oxygen tension,1,2 increased neuronal cell injury,3,4 and exacerbation of secondary cerebral damage after acute brain injury.5 In the normal brain, when hemoglobin (Hgb) concentration is <10 g/dL, active vasodilation of cerebral resistance vessels may compensate for the reduced Hgb content.6 Consequently, in the uninjured brain, brain hypoxia usually is manifest only at lower Hgb thresholds (<6 g/dL).2 However, when cerebrovascular reserve is impaired, eg, after subarachnoid hemorrhage (SAH), tissue hypoxia and cell injury theoretically may develop at higher Hgb concentrations. Consistent with this, mathematical modeling based on animal experiments of focal brain ischemia suggest that a Hgb concentration <10 g/dL is associated with an increased risk of brain tissue hypoxia.7 Correction of anemia with red blood cell transfusion8 or with Hgb carriers9,10 may therefore improve cerebral oxygenation and attenuate cell damage in animal models of brain injury.

In patients with SAH, anemia is an independent predictor of poor outcome,11 and avoidance of low Hgb is therefore warranted.12 However, the optimal Hgb threshold for red blood cell transfusion in patients with SAH remains to be better determined. Although recent clinical studies show that a Hgb concentration >11 g/dL is associated with improved outcome after SAH,13 a liberal strategy of red blood cell transfusion may in turn be associated with increased medical complications and worse clinical outcomes in brain-injured patients.14–16 In addition, in patients with acute ischemic stroke in general, and after SAH in particular, the Hgb concentration below which cerebral metabolic dysfunction may occur is still unknown.

Cerebral metabolism can be quantified at the bedside using brain tissue oxygen tension (PbtO2) monitors17 and cerebral microdialysis,18 Reduced PbtO2 levels and elevated extracellular lactate/pyruvate ratio (LPR) are sensitive and specific markers of cerebral metabolic dysfunction and correlate with poor outcome after SAH.19,20

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We sought to examine, in patients with poor-grade SAH monitored with continuous PbtO₂ monitoring and cerebral microdialysis, (1) the relationship between Hgb concentration and the levels of PbtO₂ and LPR; and (2) the threshold of Hgb concentration that was associated with an increased risk of brain hypoxia and cell energy dysfunction.

**Methods**

**Patients**

This prospective study was conducted in the Neurointensive Care Unit at the Hospital of the University of Pennsylvania, a Level I Trauma Center and Joint Commission on Accreditation of Health-care Organizations certified Stroke Center, under Institutional Review Board approval. Consecutive patients with poor-grade SAH (Hunt and Hess Grade IV or V at the time of monitoring) who underwent multimodal neuromonitoring (including intracranial pressure [ICP], PbtO₂, and cerebral microdialysis) were included in the study. Patients were monitored if their admission Glasgow Coma Scale was <8 or they later deteriorated to this level. Noncontrast cranial CT and/or lumbar puncture was used to confirm SAH. Aneurysms were verified and localized by 4-vessel cerebral angiography. On admission to the Neurointensive Care Unit, patients were stratified clinically by the Hunt and Hess scale and radiographically by the modified Fisher grade. Patients were excluded from this study if they presented with fixed and dilated pupils, had received recombinant erythropoietin, had active hemorrhage at the time of hospital admission (defined as evidence of ongoing blood loss accompanied by a decrease in the Hgb concentration of 3 g/dL in the preceding 48 hours), or had received 3 or more units of packed red cells during the month preceding admission for their SAH.

**General Management**

All patients were managed according to a standard protocol that included aggressive prehospital and intensive care unit resuscitation, early aneurysm occlusion, and aggressive prevention and treatment of intracranial hypertension and vasospasm according to intensive care unit protocols and published recommendations. Patients had CT scans on admission, after aneurysm occlusion, and on at least one subsequent occasion. Each patient received nimodipine and underwent daily transcranial Doppler examinations for vasospasm surveillance. Four-vessel cerebral angiograms were obtained during the period of maximal vasospasm risk or to confirm vasospasm. The degree of angiographic vasospasm was stratified as: mild = 1% to 24%, moderate = 25% to 50%, or severe = > 50% luminal reduction. Symptomatic vasospasm was defined by the occurrence of neurological deterioration (ie, focal deficits not present on admission or in the preceding 48 hours), or had received 3 or more units of packed red cells during the month preceding admission for their SAH.

**Blood Transfusion**

Hemoglobin concentration was measured twice per day and the decision to transfuse blood was based on the patient’s clinical status and in accordance with published guidelines. Red blood cell transfusion was not used as a primary means to expand intravascular volume.

**Multimodal Neuromonitoring**

**Brain Tissue Oxygen Tension**

PbtO₂ was measured continuously with the use of an intraparenchymal Clark-type electrode (LICOX; Integra Neurosciences, Plainsboro, NJ). Probe function and stability were confirmed by an appropriate PbtO₂ increase after an oxygen challenge (FiO2 1.0 for 5 minutes). To allow for probe equilibration, data from the first 6 hours after electrode insertion were discarded.

**Cerebral Microdialysis**

Neurochemical markers of brain metabolism were analyzed every 60 minutes with the use of a CMA 106 perfusion pump (CMA Microdialysis, Stockholm, Sweden). The CMA 106 perfusion pump (CMA Microdialysis) was used to perfuse the catheter with sterile artificial cerebrospinal fluid at a rate of 0.3 µL/min. Samples were collected every 60 minutes and analyzed for extracellular concentrations of glucose, lactate, and pyruvate with the CMA 600 analyzer (CMA Microdialysis). Sample analysis started at least 1 hour after catheter insertion to allow for normalization of changes due to probe insertion. The analyzer was automatically calibrated at the outset and every 6 hours thereafter using standard calibration solutions. ICP also was measured using an intraparenchymal monitor (Camino; Integra Neurosciences). All 3 catheters were inserted at the bedside through a burr hole into the frontal lobe and secured with a triple-lumen bolt. The various monitors were placed into brain parenchyma that appeared normal on admission head CT scan and in the vascular territory most likely to be affected by vasospasm. A noncontrast head CT scan was performed to confirm that the probes were in normal-appearing white matter. Multimodal neuromonitoring was continued for a maximum of 7 days.

**Physiological Variables**

Heart rate, mean arterial pressure (measured through an arterial catheter), central venous pressure (CVP, measured through a central venous catheter), and oxygen saturation were measured continuously in all patients using a bedside monitor (Component Monitoring System M1046–9090C; Hewlett Packard, Andover, Mass). Cerebral perfusion pressure (CPP = mean arterial pressure – ICP) was calculated. Respiratory rate, FiO₂, and ventilator settings (ventilator mode, tidal volume, minute ventilation, and positive end expiratory pressure) were recorded on intensive care unit flow sheets. Blood gas concentrations were measured simultaneously with Hgb concentration. Fluid balance also was calculated.

**Statistical Analysis**

Univariate analysis of data was performed with Student t test or Wilcoxon rank test for continuous variables as appropriate and with χ² test for categorical variables. To determine independent associations between Hgb concentrations, PbtO₂, and LPR, a multivariable forward stepwise logistic regression model was used. Brain hypoxia was defined as a PbtO₂ <20 mm Hg. An elevated LPR >40 is considered a marker of cell dysfunction and “energy crisis” secondary to hypoxia/ischemia. Accordingly, cell energy dysfunction was defined by episodes of elevated LPR >40 in the cerebral microdialysate. OR and 95% CI for PbtO₂ < 20 mm Hg and LPR >40 were adjusted for covariates based on clinical relevance, including CPP, PaO₂/FiO₂ (V/P) ratio, CVP and presence or absence of symptomatic vasospasm. Goodness of fit was assessed with the Hosmer-Lemeshow test, SPSS 16 Software (SPSS, Chicago, Ill) was used to perform statistical analysis. A probability value <0.05 was considered statistically significant.

**Results**

**Patient Characteristics**

Table 1 describes characteristics of all 20 consecutive patients with poor-grade SAH. Median age was 51 years (range, 31 to 71 years); there were 13 female and 7 male patients. Admission Hunt and Hess scale ranged from 2 to 5 and Fisher grade ranged from 2 to 4. At the time monitoring was started, all patients had a Glasgow Coma Scale <8. Intracranial monitoring started within 48 hours of SAH in all patients and lasted a median of 7 days. Eight patients (40%) developed
symptomatic vasospasm. On cerebral angiogram, one patient had severe vasospasm, 3 had moderate-to-severe vasospasm, and 4 had mild-to-moderate vasospasm. Patients with symptomatic vasospasm were treated with volume expansion and induced hypertension. Eight patients (3 with symptomatic vasospasm, 5 without symptomatic vasospasm) died.

Relationship Between Hemoglobin Concentration and Cerebral Metabolic Dysfunction in Patients With Poor-Grade Subarachnoid Hemorrhage

Physiological data measured over the entire time of intracranial monitoring are represented in Table 2. Hemoglobin concentrations (n = 206) ranged between 7.1 and 15.8 g/dL. Within each patient, the average number of episodes of brain hypoxia was significantly greater when Hgb was <9 g/dL (1.6±3) than when it was >9 g/dL (0.5±0.9, P<0.01, paired t test analysis). The proportion of hypoxic episodes in each patient was also greater when Hgb was <9 g/dL (median, 63%; interquartile range [IQR], 20% to 100%) than >9 g/dL (median, 0%; IQR, 0% to 23%; P<0.01).

The relationship between Hgb concentration and cerebral metabolic dysfunction was further examined by comparing the difference in number of episodes of brain hypoxia (PbtO2 <20 mm Hg) and cell energy dysfunction (LPR >40) according to the Hgb range. For this purpose, Hgb concentrations were categorized into 4 separate ranges: <9 g/dL (n = 39), 9 to 10 g/dL (n = 62), 10.1 to 11 g/dL (n = 51), and >11 g/dL (n = 54). Compared with other Hgb ranges, a Hgb concentration <9 g/dL at any time during the first 7 days after SAH was associated with a significant increase in the percentage of episodes of brain hypoxia and cell energy dysfunction (Figure 1). Mean absolute values of PbtO2 and LPR values, and of other important brain and systemic physiological variables (including ICP, CPP, CVP, P/F ratio, fluid balance) also were compared between an Hgb concentration <9 g/dL and Hgb values >9 g/dL (Table 3). Hgb concentrations <9 g/dL were associated with lower PbtO2 (19.9 [IQR, 7.1 to 33.1] versus 27.2 [IQR, 21.2 to 33.1] mm Hg for a Hgb concentration >9 g/dL, P=0.02), an increased incidence of hypoxic PbtO2 values (52% versus 21%, P<0.01), a higher LPR (36 [IQR, 25 to 59] versus 29 [IQR, 25 to 38], P=0.16), and an increased percentage of LPR episodes >40 (43% versus 23%, P=0.03). The other

Table 1. Patient Characteristics

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<th>Outcome</th>
<th>Start of Monitoring, Days</th>
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H&H indicates Hunt and Hess scale; F, female; M, male; ACoA, anterior communicating artery; ICA, internal carotid artery; MCA, middle cerebral artery; VB, verteobasilar system; PCoA, posterior communicating artery; D, death; S, survival. Time to start of multimodality monitoring (ICP, PbtO2, and cerebral microdialysis) is given in days after SAH. See “Methods” for definition of symptomatic vasospasm.

Table 2. Physiological Data

<table>
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<tr>
<th>Variable</th>
<th>Value</th>
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</thead>
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<td>ICP, mm Hg</td>
<td>10 (5–15)</td>
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<tr>
<td>CPP, mm Hg</td>
<td>93 (75–113)</td>
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<tr>
<td>CVP, cm H₂O</td>
<td>8 (5–11)</td>
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<tr>
<td>PaO₂/FIO₂ ratio</td>
<td>247 (101–378)</td>
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<td>Hgb, g/dL</td>
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<tr>
<td>LPR</td>
<td>28 (25–34)</td>
</tr>
<tr>
<td>PbtO₂, mm Hg</td>
<td>28.3 (23.1–34.7)</td>
</tr>
</tbody>
</table>

Data are expressed as median with interquartile range in parentheses, except otherwise stated.
variables, including ICP, CPP, CVP, P/F ratio, and fluid balance, were similar across the Hgb ranges.

**Hemoglobin Concentration <9 g/dL Independently Predicts Cerebral Metabolic Dysfunction in Patients With Poor-Grade Subarachnoid Hemorrhage**

Compared with patients without symptomatic vasospasm (n = 12), those who had symptomatic vasospasm (n = 8) had significantly lower mean Hgb concentration (10.6±1.6 versus 9.7±1.1 g/dL, P<0.01). However, although the trends over time differed, a close relationship between Hgb concentration and levels of LPR and PbtO2 was observed within each group (Figure 2). To further analyze this relationship, a multivariable logistic regression model was used. Hemoglobin concentration <9 g/dL was entered in the model as a categorical variable, and OR and 95% CIs for brain hypoxia (PbtO2 <20 mm Hg) and cell energy dysfunction (LPR >40) were adjusted for presence or absence of symptomatic vasospasm, CPP, CVP, and P/F ratio. Using this model, a hemoglobin concentration <9 g/dL was independently associated with an increased risk of tissue hypoxia (adjusted OR, 7.92; 95% CI, 2.32 to 27.09; P<0.01) and of cell energy dysfunction (adjusted OR, 4.24; 95% CI, 1.33 to 13.55; P=0.02; Table 4).

**Discussion**

In this prospective study, we used cerebral microdialysis and brain oxygen monitors to examine the relationship between Hgb concentration and cerebral metabolic dysfunction in 20 patients with poor-grade SAH. The results of our preliminary study show that: (1) in patients with poor-grade SAH, there was a relationship between Hgb concentration and levels of PbtO2; and neurochemical markers of cell metabolism; (2) the incidence of brain hypoxia and cell energy dysfunction increased significantly when Hgb was <9 g/dL; and (3) the association between reduced Hgb concentration (<9 g/dL) and increased risk of brain hypoxia and cell energy dysfunction was independent of other important physiological variables (CPP, CVP, and P/F ratio) and from the presence of symptomatic vasospasm. These data suggest that a reduced Hgb concentration (<9 g/dL) is associated with a significant and independent increase in the risk of cerebral metabolic dysfunction in patients with poor-grade SAH.

Several experimental studies show that reduced Hgb concentrations are associated with tissue hypoxia, impaired autoregulation, and increased cellular injury in the brain. In animals without acute brain injury, the incidence of cerebral hypoxia only increases significantly once Hgb concentrations are <6 g/dL. In these animals, active compensatory vasodilation, that starts when the Hgb level is between 9 and 10 g/dL, prevents the normal brain from further injury. However, when cerebrovascular reserve is impaired, eg, after SAH, cerebral hypoxia may theoretically occur at higher Hgb concentrations. Indeed, one study that used mathematical modeling suggested that a Hgb concentration <10 g/dL was associated with an increased risk of brain damage in animals with focal cerebral ischemia. Whether the same results obtained in focal ischemia apply in more diffuse processes or global ischemia is only beginning to be elucidated. In particular, the ideal Hgb target to prevent further cerebral damage after acute brain injury remains to be better established in vivo in humans.

In this preliminary study using PbtO2 monitoring and cerebral microdialysis, we found that a Hgb concentration <9 g/dL after SAH was associated with a significant increase in the incidence of tissue hypoxia and cell energy dysfunction. The increase in cerebral metabolic dysfunction appeared to be unrelated to concomitant changes in other important physiological parameters that may influence cellular oxygenation and metabolism in the brain, because variables, including ICP, CPP, CVP, P/F ratio, and fluid balance, were similar

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hgb &lt;9 g/dL</th>
<th>Hgb &gt;9 g/dL</th>
<th>P Value</th>
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<tr>
<td>PbtO2, mm Hg</td>
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<td>27.2 (21.2–33.1)</td>
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<tr>
<td>LPR &gt;40, %</td>
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<td>23</td>
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<td>11 (6–15)</td>
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<tr>
<td>CPP, mm Hg</td>
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<td>Fluid balance, mL</td>
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Data are presented as median (interquartile range).
across the various examined Hgb concentrations on univariate analysis (Table 3).

Forty percent of the patients in our study cohort developed symptomatic vasospasm (confirmed on angiogram) and were treated with volume expansion and induced hypertension. In this subset of patients, the observed reduced Hgb concentrations may be partially related to hemodilution. Although this hemodilution may optimize blood rheology, hemodilutional anemia has been shown in some experimental models of severe brain injury to impair brain tissue oxygenation and increase secondary brain damage. Recent clinical studies have demonstrated that hypervolemia and hemodilution when used as part of triple-H therapy after SAH may negatively affect PbtO2. Although the underlying pathophysiological mechanisms by which this may occur are not well understood, one plausible hypothesis is that hemodilution may reduce brain tissue oxygen by causing a decrease in Hgb concentration. Volume expansion and induced hypertension may also impair lung oxygenation and alter CPP levels.

Irrespective of the presence or absence of symptomatic vasospasm, we found a close relationship between changes in Hgb concentrations and PbtO2 levels over time (Figure 2). To more completely address this issue, associations between reduced Hgb concentration and increased cerebral tissue injury were adjusted for CPP, CVP, P/F ratio, and the presence of symptomatic vasospasm using a multivariable logistic regression model. This analysis showed that an Hgb concentration $\leq 9$ g/dL was significantly associated with an increased risk of brain tissue hypoxia and cell energy dysfunction even after adjusting for these covariates (Table 4). This suggests that a low Hgb concentration may be per se an independent cause of cerebral metabolic dysfunction after SAH. Finally, our results appear to be consistent with recent clinical studies that suggest a Hgb concentration $\leq 9$ g/dL may be a precipitating factor in patients with acute ischemic stroke.

**Figure 2.** Line graphs illustrating means±SD over time (Day 1 to 7 of intracranial monitoring) of Hgb concentrations with the corresponding PbtO2 and cerebral microdialysate LPR in patients with poor-grade SAH with and without symptomatic vasospasm.

**Table 4.** Independent Associations Between Hgb Concentration and PbtO2 ($\leq 20$ mm Hg) and Cell Energy Dysfunction (LP ratio $\geq 40$) in Patients With SAH

<table>
<thead>
<tr>
<th>Variable</th>
<th>PbtO2 $&lt;20$ mm Hg, OR (95% CI)</th>
<th>$P$</th>
<th>LP Ratio $&gt;40$, OR (95% CI)</th>
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<td>Hgb $&lt;9$ g/dL</td>
<td>7.92 (2.32–27.09)</td>
<td>$&lt;0.01$</td>
<td>4.24 (1.33–13.55)</td>
<td>0.02</td>
</tr>
<tr>
<td>CPP</td>
<td>0.99 (0.97–1.01)</td>
<td>0.21</td>
<td>0.98 (0.96–1.01)</td>
<td>0.14</td>
</tr>
<tr>
<td>CVP</td>
<td>0.87 (0.76–0.98)</td>
<td>0.03</td>
<td>0.88 (0.78–0.99)</td>
<td>0.04</td>
</tr>
<tr>
<td>PaO2/FIO2 ratio</td>
<td>0.98 (0.97–0.99)</td>
<td>$&lt;0.01$</td>
<td>0.99 (0.95–1.01)</td>
<td>0.16</td>
</tr>
<tr>
<td>Symptomatic vasospasm</td>
<td>4.13 (1.33–12.83)</td>
<td>0.01</td>
<td>3.87 (1.33–11.23)</td>
<td>0.01</td>
</tr>
</tbody>
</table>
Given the small patient number (n=20), our results should be regarded as preliminary. However, we examined multiple physiological variables and corresponding Hgb concentrations from >200 time points with robust statistical methods. The physiological findings therefore are compelling and suggest that a concentration of Hgb <9 g/dL is associated with a significant increase in the risk of cerebral metabolic dysfunction. These results support the concept that anemia-induced brain injury may contribute to worse clinical outcome in patients with SAH. Indeed, recent studies support this hypothesis showing that anemia is associated with poor outcome after SAH.11 However, the optimal Hgb target for blood transfusion in patients with SAH is poorly defined and it remains unclear how to balance the risks of anemia with those of transfusion. Recent single-center studies suggest that the maintenance of Hgb concentrations >11 g/dL may improve outcome after SAH.18,31 This would implicate that a liberal strategy for red blood cell transfusion may be indicated in SAH, although whether this applies to all patients, ie, those with and without adequate cerebrovascular reserve, is unclear. Furthermore, these results are in contrast to several studies conducted in critically ill nonneurological patients32–37 and in patients with severe brain injury14–16 that showed that a liberal strategy of red blood cell transfusion to maintain Hgb concentrations >10 g/dL do not confer any significant advantage to patient outcome when compared with a more restrictive transfusion strategy (Hgb target 7 to 9 g/dL). Morbidity and mortality may even further increase when transfused red cells are stored for more than 2 weeks.38 Taken together, these data indicate that the ideal Hgb range for the clinical management of patients with SAH is yet unknown. Although our data do not allow us to make a single recommendation about transfusion thresholds in all patients with SAH, this study suggests that reduced Hgb concentration <9 g/dL may contribute to further exacerbate secondary brain injury in patients with poor-grade SAH. Additional studies are needed to confirm these findings and to precisely determine the optimal Hgb threshold for blood transfusion in all patients with SAH.

Summary
This prospective observational study using continuous cerebral microdialysis and brain oxygen monitoring demonstrates that an Hgb concentration <9 g/dL is strongly associated with an increased incidence of brain hypoxia and cell energy dysfunction in patients with poor-grade aneurysmal SAH. These preliminary findings suggest that the maintenance of Hgb concentrations >9 g/dL may prevent further secondary brain injury after poor-grade aneurysmal SAH.

Sources of Funding
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Disclosures
None.

References
8. Rigamonti A, McLaren AT, Mazer CD, Nix K, Ragoonanan T, Freedman J, Harrington A, Hare GM. Storage of strain-specific rat blood limits the physiological findings therefore are compelling and corresponding Hgb concentrations from >200 time points with robust statistical methods. The physiological findings therefore are compelling and suggest that a concentration of Hgb <9 g/dL is associated with a significant increase in the risk of cerebral metabolic dysfunction. These results support the concept that anemia-induced brain injury may contribute to worse clinical outcome in patients with SAH. Indeed, recent studies support this hypothesis showing that anemia is associated with poor outcome after SAH.11 However, the optimal Hgb target for blood transfusion in patients with SAH is poorly defined and it remains unclear how to balance the risks of anemia with those of transfusion. Recent single-center studies suggest that the maintenance of Hgb concentrations >11 g/dL may improve outcome after SAH.18,31 This would implicate that a liberal strategy for red blood cell transfusion may be indicated in SAH, although whether this applies to all patients, ie, those with and without adequate cerebrovascular reserve, is unclear. Furthermore, these results are in contrast to several studies conducted in critically ill nonneurological patients32–37 and in patients with severe brain injury14–16 that showed that a liberal strategy of red blood cell transfusion to maintain Hgb concentrations >10 g/dL do not confer any significant advantage to patient outcome when compared with a more restrictive transfusion strategy (Hgb target 7 to 9 g/dL). Morbidity and mortality may even further increase when transfused red cells are stored for more than 2 weeks.38 Taken together, these data indicate that the ideal Hgb range for the clinical management of patients with SAH is yet unknown. Although our data do not allow us to make a single recommendation about transfusion thresholds in all patients with SAH, this study suggests that reduced Hgb concentration <9 g/dL may contribute to further exacerbate secondary brain injury in patients with poor-grade SAH. Additional studies are needed to confirm these findings and to precisely determine the optimal Hgb threshold for blood transfusion in all patients with SAH.

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