Intracranial Pressure After Subarachnoid Hemorrhage*

Tommaso Zoele, MD1; Alessandra Lombardo, MD1,2; Angelo Colombo, MD1; Luca Longhi, MD1,2; Elisa R. Zanier, MD1; Paolo Rampini, MD4; Nino Stocchetti, MD1,2

Objectives: To describe mean intracranial pressure after aneurysmal subarachnoid hemorrhage, to identify clinical factors associated with increased mean intracranial pressure, and to explore the relationship between mean intracranial pressure and outcome.

Design: Analysis of a prospectively collected observational database.

Setting: Neuroscience ICU of an academic hospital.

Patients: One hundred sixteen patients with subarachnoid hemorrhage and intracranial pressure monitoring.

Interventions: None.

Measurements and Main Results: Episodes of intracranial pressure greater than 20 mm Hg lasting at least 5 minutes and the mean intracranial pressure for every 12-hour interval were analyzed. The highest mean intracranial pressure was analyzed in relation to demographic characteristics, acute neurologic status, initial radiological findings, aneurysm treatment, clinical vasospasm, and ischemic lesion. Mortality and 6-month outcome (evaluated using a dichotomized Glasgow Outcome Scale) were also introduced in multivariable logistic models. Eighty-one percent of patients had at least one episode of high intracranial pressure and 36% had a highest mean intracranial pressure more than 20 mm Hg. The number of patients with high intracranial pressure peaked 3 days after subarachnoid hemorrhage and declined after day 7. Highest mean intracranial pressure greater than 20 mm Hg was significantly associated with initial neurologic status, aneurysmal rebleeding, amount of blood on CT scan, and ischemic lesion within 72 hours from subarachnoid hemorrhage. Patients with highest mean intracranial pressure greater than 20 mm Hg had significantly higher mortality. When death, vegetative state, and severe disability at 6 months were pooled, however, intracranial pressure was not an independent predictor of unfavorable outcome.

Conclusions: High intracranial pressure is a common complication in the first week after subarachnoid hemorrhage in severe cases admitted to ICU. Mean intracranial pressure is associated with the severity of early brain injury and with mortality. (Crit Care Med 2015; 43:168–176)

Key Words: brain injury; Glasgow Outcome Scale; intracranial aneurysm; intracranial pressure; mortality; subarachnoid hemorrhage

Aneurysmal subarachnoid hemorrhage (SAH) has severe consequences, with mortality around 50% and good functional recovery in only one third of survivors (1). Among the multiple brain injury mechanisms after SAH, high intracranial pressure (HICP) may play an important role (2). Animal experiments have shown that the intracranial bleeding causes an intracranial pressure (ICP) surge, lower cerebral perfusion pressure (CPP), and global ischemia (3). In patients, this mechanism may contribute to sudden death before hospital admission (12% of patients) (4). Elevated ICP has also been noted in the first week after SAH (5, 6).

Different mechanisms may raise ICP, such as global brain edema due to initial ischemia, intracerebral hematoma (ICH), cerebral infarction, acute and delayed hydrocephalus, or impaired cerebral autoregulation, occurring at different times during the hospital stay (7). Microdialysis studies have identified markers of brain metabolic crisis, leading to poor outcome, associated with HICP (8). Information about risk factors related to HICP after SAH and its time patterns is limited, especially in patients treated with endovascular coiling.

We put forward the following hypotheses: 1) HICP after SAH is common and not limited to the first hours after...
bleeding; 2) specific clinical and radiological findings may be associated with the risk of HICP; 3) HICP affects the outcome. We therefore studied 116 patients with SAH in order to track mean ICP changes after bleeding, to identify clinical factors associated with mean ICP greater than 20 mm Hg, and to explore the relationship between ICP and outcome.

**MATERIALS AND METHODS**

**Patients and Clinical Management**

We retrospectively examined a prospective observational database; data were collected from July 2005 to February 2012 at the Neuroscience ICU, and the study was approved by the Ethics Committee of the Fondazione IRCCS Ca’ Granda–Ospedale Maggiore Policlinico. Inclusion criteria were diagnosis of aneurysmal SAH, ICP monitored for more than 12 hours, and age older than 18 years.

Patients with SAH were managed according to international recommendations (9). After stabilization, the SAH diagnosis was confirmed in all patients by a CT scan followed by angiography or CT angiography. Management included early clipping or coiling of the aneurysm and surgical evacuation of the ICH where indicated. Acute symptomatic hydrocephalus was treated by drainage of the cerebrospinal fluid (CSF) through an external ventricular drain (EVD). EVD and CSF drainage are managed complying the following protocol based on radiological and clinical characteristics of patients:

- Patients with normal ICP (ICP $\leq 20$ mm Hg and no ICP therapy) and without hydrocephalus: EVD closed.
- Patients with controlled ICP (ICP $\leq 20$ mm Hg with standard medical therapy) and/or radiological signs of hydrocephalus: EVD opened during the first 10 minutes of every hour.
- Patients with high ICP (ICP $> 20$ mm Hg or maximal medical therapy) with or without radiological signs of hydrocephalus: EVD opened the first 50 minutes of every hour.
- In case of catheter obstruction and ICP-impaired waveform, a new EVD or an intraparenchymal probe is placed after CT scan and neurosurgeon consultation.

Patients were not given anticonvulsive prophylaxis. Hemoglobin levels were monitored at least twice daily and transfusion threshold was 9 g/dL. Oral nimodipine was given only if the first dose did not cause arterial hypotension. A second CT scan was taken within the first 72 hours after treatment of the aneurysm to identify complications. In case of clinical vasospasm, angioplasty or intra-arterial papaverine infusion was employed in patients refractory to medical treatment (blood pressure rise after optimization of intravascular volume). Clinical vasospasm was defined as neuroworsening associated with angiographic confirmation of vasospasm (arterial diameter narrowing $> 20\%$ from baseline). In our patients, neurologic status was monitored at least six times a day by the medical staff until discharge from the ICU. Neuroworsening was defined as loss of one point of the Glasgow Coma Scale (GCS, evaluating both side of the body for the motor component) and/or the presence of new focal deficits. In case the neuroworsening was not attributed to systemic complications, patients were subjected to a new CT scan or MRI to rule out hydrocephalus/rebleeding and therefore to angiography (10).

**ICP Monitoring and Treatment**

ICP (a ventricular drain was placed in 93% of patients) was monitored in severe, comatose patients and/or cases with acute hydrocephalus. Patients were positioned with a slight head elevation (15–20°); ICP and arterial pressure transducers were zeroed with the external acoustic meatus as reference point for calculating CPP. ICP data were filtered and analyzed as previously described (11). Briefly, data were analyzed twice a day at 12-hour intervals (from 8 AM to 8 PM and from 8 PM to 8 AM). ICP values obtained during CSF drainage, suction, and short-acting nursing were filtered and not considered during mean ICP calculations. After filtering, episodes of HICP (ICP $> 20$ mm Hg for at least 5 min) were noted. The mean ICP for the 12-hour interval was calculated and indicated as “mean ICP” When monitoring was concluded, the highest mean ICP for each patient was classified as “highest mean ICP.” CPP was calculated as mean arterial pressure minus ICP. As for ICP, we noted the mean for the 12-hour interval, calling it “mean CPP.”

When monitoring was concluded, the lowest mean CPP from each patient was classified as “lowest mean CPP.” In our center, ICP probes are removed after 24 hours of ICP less than or equal to 20 mm Hg without any ICP treatment (including CSF drainage) after medical round at 8 AM or 8 PM.

The aim of therapy was to keep ICP below 20 mm Hg and CPP above 65 mm Hg. ICP therapy intensity was classified as follows:

- Standard medical therapy: sedation, mannitol, CSF withdrawal, mandatory mechanical ventilation to obtain $P_{A\text{CO}_2}$ 30–35 mm Hg, plasma Na higher than 140 mEq/L.
- Maximal medical therapy: $P_{A\text{CO}_2}$ less than 30 mm Hg, barbiturates, hypothermia.
- Surgical therapy: ICH evacuation and/or decompression.

ICP therapy was defined as “low intensity” (standard medical therapy) or “high intensity” (maximal medical therapy and/or surgery) for statistical analysis.

**Clinical Variables**

The database included age, sex, neurologic status, surgical/endo-vascular treatment of the aneurysm, treatment complications (including intraoperative rebleeding, prolonged temporary clipping, surgical/endovascular arterial occlusion, and thromboembolic event), rebleeding, perioperative hypoxia defined as $Sp_{O2}$ less than 90%, hypotension defined as systolic blood pressure less than 90 mm Hg, ICP therapy, clinical vasospasm and outcome, episodes of anemia (hemoglobin $< 9$ g/dL), and infection. Neurologic status was assessed according to the World Federation of Neurological Surgeons grading scale (WFNS) and classified as severe (WFNS, 4–5) or mild (WFNS, 1–3) (12) before and after treatment of the aneurysm. Survival and 6-month Glasgow Outcome Scale (GOS) (13) were considered as clinical outcomes.
Scores were considered favorable (4–5) or unfavorable (1–3). Sixth month outcome was obtained through phone structured interviews by medical staff as suggested by Wilson et al (14).

Radiological Variables

Admission and follow-up CT scans were examined independently by two of the authors. Presence of midline shift greater than 5 mm and ICH were recorded. The amount of blood in the scans was assessed using the Fisher scale (15). Hydrocephalus was assessed by ventriculocranial ratio (16). Early lesions were defined as hypodense lesions visible on the CT taken within 72 hours from SAH; hypodense lesions occurring after this time were called “delayed lesions.” For statistical analysis, patients were initially classified as with or without early lesion. Additionally, they were dichotomized as with or without lesion at any time (Supplementary Fig. 1, Supplemental Digital Content 1, http://links.lww.com/CCM/B83).

The location of the aneurysm and the presence of angiographic vasospasm were assessed by certified neuroradiologists.

Table 1. Patients’ Clinical and Radiologic Characteristics

| Variable                                      | n (%)       |
|-----------------------------------------------|-------------|
| Female                                        | 86 (74)     |
| Age (mean ± sd)                               | 57 ± 13     |
| Neurologic status before aneurysm treatment   |             |
| WFNS 1                                        | 17 (15)     |
| WFNS 2                                        | 24 (21)     |
| WFNS 3                                        | 8 (7)       |
| WFNS 4                                        | 33 (28)     |
| WFNS 5                                        | 34 (29)     |
| Neurologic status after aneurysm treatment    |             |
| WFNS 1                                        | 7 (6)       |
| WFNS 2                                        | 13 (12)     |
| WFNS 3                                        | 2 (2)       |
| WFNS 4                                        | 58 (51)     |
| WFNS 5                                        | 33 (29)     |
| Fisher grade                                  |             |
| 1                                             | 0           |
| 2                                             | 2 (2)       |
| 3                                             | 85 (73)     |
| 4                                             | 29 (25)     |
| Intracerebral hematoma                        | 53 (46)     |
| Hydrocephalus                                 | 64 (55)     |
| Rebleeding                                    | 46 (39)     |
| Shift > 5 mm                                  | 24 (20)     |
| Perioperative hypoxia                         | 10 (8)      |
| Perioperative hypotension                     | 18 (15)     |
| Hemoglobin < 9 g/dL                           | 47 (40)     |
| Infection                                     | 69 (59)     |
| Aneurysm treatment                            |             |
| Endovascular                                  | 84 (72)     |
| Surgical                                      | 29 (25)     |
| None                                          | 3 (3)       |
| Treatment complication                        | 61 (52)     |
| Aneurysm location                             |             |
| Anterior circulation                          | 94 (81)     |
| Posterior circulation                         | 22 (19)     |
| Clinical vasospasm                            | 34 (29)     |
| CT hypodense lesion                           |             |
| Early lesion                                  | 82 (71)     |
| Delayed lesion                                | 55 (47)     |
| None                                          | 18 (15)     |

(Continued)

Table 1. (Continued). Patients’ Clinical and Radiologic Characteristics

| Variable                                      | n (%)       |
|-----------------------------------------------|-------------|
| ICP                                           |             |
| Patients with episodes of high intracranial pressure \* | 94 (81)     |
| Patients with highest mean ICP > 20 mm Hg      | 42 (36)     |
| ICP treatment                                 |             |
| Low intensity                                 | 80 (69)     |
| High intensity                                | 36 (31)     |
| Therapeutic Paco₂ < 35 mm Hg                  | 63 (54)     |
| Deaths in ICU                                 | 25 (21)     |
| Glasgow Outcome Scale at sixth month          |             |
| 1                                             | 35 (32)     |
| 2                                             | 4 (4)       |
| 3                                             | 42 (39)     |
| 4                                             | 7 (6)       |
| 5                                             | 20 (19)     |
| Missing                                       | 8           |

WFNS = World Federation of Neurological Surgeons grading scale, ICP = intracranial pressure.

\*ICP > 20 mm Hg for at least 5 min.

Scores were considered favorable (4–5) or unfavorable (1–3). Sixth month outcome was obtained through phone structured interviews by medical staff as suggested by Wilson et al (14).
relationship between ICP and outcomes using a restricted spline function and linearity Wald test. Since the Wald test was not significant, the relationship was considered linear.

Three binary logistic regression models were built, with mean ICP greater than 20 mm Hg, mortality, and unfavorable outcome as dependent variables. Initially, all the variables with \( p \) value less than 0.20 in univariate analysis were entered in the models as independent variables, then a backward stepwise selection method was used until all the remaining variables were significantly associated. Cases with missing values for any of the variables in the model were omitted. Finally, to assess the model adequacy, we used the Cessie-van Houwelingen statistics (an improvement on the Hosmer-Lemeshow test for goodness of fit) and \( R^2 \) statistics. To assess discrimination, we calculated the area under receiver operating characteristic curve (c). Kaplan-Meier survival curves were compared using a log-rank test to assess the difference between patients with and without highest mean ICP greater than 20 mm Hg; \( p \) less than 0.05 was considered significant.

Analyses were done using R (version 2.15.1, 2012 The R Foundation for Statistical Computing, Vienna, Austria) and Prism 4 software (version 4.01, Graph-Pad Software, San Diego, CA).

**RESULTS**

**General Data**

Out of 265 patients consecutively admitted, 116 fulfilled the inclusion criteria; 144 were excluded because ICP was not monitored and five because complete imaging data were not available. Patients’ main details are reported in Table 1. Mean age was 57 years (± SD 13) and 74% were female. Most were in poor neurologic condition at admission, with 80% classified as WFNS 4–5 after aneurysm treatment. Ruptured aneurysms were coiled or clipped (72% and 25%, respectively) within 48 hours from admission in all but one patient. In three patients with GCS 3 and no brainstem reflexes, the aneurysm was not treated. Ninety-eight percent presented massive SAH and were classified as Fisher 3 (73%) or 4 (25%). Hydrocephalus was found in 55% of patients. ICH was detected in 46% with a midline shift greater than 5 mm in 20%. A CT early lesion was detected in 71% of patients and 47% developed a CT delayed lesion. Clinical vasospasm was observed in 29% cases. Fifty-nine percent of patients developed an infection, but none of them had acute respiratory distress syndrome, septic shock, or multiple organ failure. Forty percent of subjects developed at least one episode of hemoglobin less than 9 g/dL.

Six months from the SAH (GOS, 4–5), 32% percent of patients were dead and only 25% had a favorable outcome. Eight patients were lost to follow-up.

**Intracranial Hypertension Prevalence and Time Course**

Median length of monitoring was 5.5 days (range, 0.5–15 d), with a total of 17,088 hours monitored during the study. In 93% of patients, ICP was monitored using a ventricular catheter while in the others using subdural catheter. Eighty-one percent of patients had at least one episode of HICP, and 36% had a highest mean ICP higher than 20 mm Hg; the median of the highest mean ICP was 18 mm Hg (range, 6–96 mm Hg).
For 69%, standard medical therapy was used to control ICP, and in 13%, it was combined with evacuation of the ICH. In the remaining patients, maximal medical therapy (5%), surgical decompression (11%), or both (2%) were used.

The number of patients with mean ICP greater than 20 mm Hg or with episodes of HICP peaked on day 3 after SAH, slightly decreasing over the next days (Fig. 1). On day 7, the number of patients with mean ICP greater than 20 mm Hg was still similar to day 1.

Factors Associated With High ICP

Neurologic status, rebleeding, CT early lesions, and CT lesions at any time were significantly related with univariate analysis (Table 2). In the multivariable model, only the neurologic status evaluated before aneurysm treatment, rebleeding, CT early

### TABLE 2. Univariate Analysis for Factors Related to Highest Mean Intracranial Pressure Greater Than 20 mm Hg

| Variable                      | Patients With Highest Mean ICP < 20 mm Hg | Patients With Highest Mean ICP > 20 mm Hg | p     |
|-------------------------------|------------------------------------------|------------------------------------------|-------|
| Age (mean ± sd)               | 59 ± 13                                  | 54 ± 13                                  | 0.06  |
| Sex                           |                                          |                                          | 0.18  |
| Female                        | 58                                        | 28                                       |       |
| Male                          | 16                                        | 14                                       |       |
| Fisher                        |                                          |                                          | 0.19  |
| 3                             | 51                                        | 34                                       |       |
| 2 and 4                       | 23                                        | 8                                        |       |
| Shift > 5 mm                  |                                          |                                          | 0.15  |
| Yes                           | 12                                        | 12                                       |       |
| No                            | 62                                        | 30                                       |       |
| Intracerebral hematoma        |                                          |                                          | 0.33  |
| Yes                           | 31                                        | 22                                       |       |
| No                            | 43                                        | 20                                       |       |
| Hydrocephalus                 |                                          |                                          | 0.70  |
| Yes                           | 42                                        | 22                                       |       |
| No                            | 32                                        | 20                                       |       |
| Aneurysm treatment            |                                          |                                          | 1     |
| Coiling                       | 55                                        | 29                                       |       |
| Clipping                      | 19                                        | 10                                       |       |
| Complication                  |                                          |                                          | 0.55  |
| Yes                           | 38                                        | 23                                       |       |
| No                            | 36                                        | 16                                       |       |
| Neurologic status before treatment |                                      |                                          | < 0.001 |
| Mild                          | 40                                        | 9                                        |       |
| Severe                        | 34                                        | 33                                       |       |
| Neurologic status after treatment |                                      |                                          | 0.02  |
| Mild                          | 19                                        | 3                                        |       |
| Severe                        | 55                                        | 36                                       |       |
| Rebleeding                    |                                          |                                          | 0.01  |
| Yes                           | 23                                        | 23                                       |       |
| No                            | 51                                        | 19                                       |       |
| CT early lesion               |                                          |                                          | < 0.001 |
| Yes                           | 45                                        | 37                                       |       |
| No                            | 29                                        | 5                                        |       |

ICP = intracranial pressure.

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The number of patients with mean ICP greater than 20 mm Hg or with episodes of HICP peaked on day 3 after SAH, slightly decreasing over the next days (Fig. 1). On day 7, the number of patients with mean ICP greater than 20 mm Hg was still similar to day 1.

### TABLE 2. (Continued). Univariate Analysis for Factors Related to Highest Mean Intracranial Pressure Greater Than 20 mm Hg

| Variable                      | Patients With Highest Mean ICP < 20 mm Hg | Patients With Highest Mean ICP > 20 mm Hg | p     |
|-------------------------------|------------------------------------------|------------------------------------------|-------|
| Clinical vasospasm            |                                          |                                          | 0.39  |
| Yes                           | 24                                        | 10                                       |       |
| No                            | 50                                        | 32                                       |       |
| Aneurysm location             |                                          |                                          | 0.22  |
| Anterior                      | 57                                        | 37                                       |       |
| Posterior                     | 17                                        | 5                                        |       |
| CT lesion at any time         |                                          |                                          | 0.01  |
| Yes                           | 58                                        | 40                                       |       |
| No                            | 16                                        | 2                                        |       |
| Perioperative hypoxia         |                                          |                                          | 0.49  |
| Yes                           | 5                                         | 5                                        |       |
| No                            | 69                                        | 37                                       |       |
| Perioperative hypotension     |                                          |                                          | 0.79  |
| Yes                           | 11                                        | 7                                        |       |
| No                            | 63                                        | 35                                       |       |
| Hemoglobin < 9 g/dL           |                                          |                                          | 0.02  |
| Yes                           | 24                                        | 23                                       |       |
| No                            | 50                                        | 19                                       |       |
| Infection                     |                                          |                                          | 0.44  |
| Yes                           | 46                                        | 23                                       |       |
| No                            | 28                                        | 19                                       |       |

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Factors Associated With High ICP

Neurologic status, rebleeding, CT early lesions, and CT lesions at any time were significantly related with univariate analysis (Table 2). In the multivariable model, only the neurologic status evaluated before aneurysm treatment, rebleeding, CT early
lesions, and Fisher grade were significantly related with highest mean ICP greater than 20 mm Hg (Table 3). Indicators of model performance showed $R^2 = 0.31$, goodness of fitness with $p = 0.09$ and $c = 0.77$.

### Relationship Between ICP and Outcomes

Patients with highest mean ICP greater than 20 mm Hg had higher mortality (Fig. 2). Most deaths occurred in the first 7 days after SAH. There was a linear relationship between highest mean ICP and mortality (Supplementary Fig. 2, Supplemental Digital Content 1, http://links.lww.com/CCM/B83). In addition, sex, neurologic status after treatment, CT lesion at any time, highest mean ICP, and ICP therapy intensity were significantly related with unfavorable outcome at 6 months; in the multivariable analysis, factors such as age, neurologic status, early ischemic lesion, and poor neurologic status. HICP prolonged HICP were the amount of blood on CT scan, rebleeding, early ischemic lesion, and poor neurologic status. HICP therefore seems related to the severity of early brain injury. Our data did not show any relationship between HICP and hydrocephalus probably due to the high prevalence of EVD placement and CSF drainage based on radiological signs or clinical suspicion of this common complication. However, while ICP in mild patients was well controlled with CSF withdrawal, severe patients required a more aggressive treatment (Supplementary Result 1, Supplemental Digital Content 1, http://links.lww.com/CCM/B83). This finding suggests that in the severe group, CSF drainage is not enough to control HICP, which is likely to be related to other causes (as global ischemia secondary to aneurysm bleeding, early ischemic lesions, etc.) rather than solely to CSF circulation disturbances. We were not able to show any significant relationship between ICP and clinical vasospasm even though a substantial number of patients had HICP up to day 7; probably cerebral ischemia due to vasospasm was not enough to cause HICP, independent of other predictors.

HICP was associated with more deaths, mainly in the ICU; in those patients, HICP was probably a final common pathway to death. Our data, however, showed no relationship between

### Table 3. Multivariable Model for Highest Mean Intracranial Pressure Greater Than 20 mm Hg

| Variable                              | OR (95% CI)     | p   |
|---------------------------------------|-----------------|-----|
| Neurologic status before aneurysm treatment (severe vs mild) | 3.71 (1.42–9.66) | 0.007 |
| Rebleeding (yes vs no)                | 3.47 (1.38–8.69) | 0.008 |
| Fisher grade (2–4 vs 3)               | 0.29 (0.09–0.87) | 0.027 |
| CT early lesion (yes vs no)           | 4.32 (1.37–13.57) | 0.012 |

OR = odds ratio.

Figure 2. Kaplan-Meier survival curves for patients with highest mean intracranial pressure (ICP) less than or equal to 20 mm Hg, between 20 and 30 mm Hg, and higher than 30 mm Hg. Log-rank test $p < 0.01$. SAH = subarachnoid hemorrhage.

### DISCUSSION

In this study, HICP was common after SAH, but more frequent in patients with severe brain injury, and was associated with higher mortality. HICP episodes occurred in 80% of our cases, and more than one third had sustained HICP, lasting more than 12 hours, despite conventional and aggressive treatment. This confirms results from other groups (5, 6). ICP was still high in a considerable number of patients until day 7 after bleeding.

In the multivariable analysis, the independent predictors of prolonged HICP were the amount of blood on CT scan, rebleeding, early ischemic lesion, and poor neurologic status. HICP therefore seems related to the severity of early brain injury. Our data did not show any relationship between HICP and hydrocephalus probably due to the high prevalence of EVD placement and CSF drainage based on radiological signs or clinical suspicion of this common complication. However, while ICP in mild patients was well controlled with CSF withdrawal, severe patients required a more aggressive treatment (Supplementary Result 1, Supplemental Digital Content 1, http://links.lww.com/CCM/B83). This finding suggests that in the severe group, CSF drainage is not enough to control HICP, which is likely to be related to other causes (as global ischemia secondary to aneurysm bleeding, early ischemic lesions, etc.) rather than solely to CSF circulation disturbances. We were not able to show any significant relationship between ICP and clinical vasospasm even though a substantial number of patients had HICP up to day 7; probably cerebral ischemia due to vasospasm was not enough to cause HICP, independent of other predictors.

HICP was associated with more deaths, mainly in the ICU; in those patients, HICP was probably a final common pathway to death. Our data, however, showed no relationship between

### Table 5. Model performance showed $R^2 = 0.47$, goodness of fit with $p = 0.96$ and $c = 0.87$.

### CPP After SAH

The median of the lowest mean CPP was 68 mm Hg (range, 5–104 mm Hg); in 56%, the lowest mean CPP was more than 65 mm Hg. In 31 out 42 patients (74%), highest mean ICP greater than 20 mm Hg was associated with mean CPP lower than 65 mm Hg.

Neurologic status, CT early lesions, CT lesions at any time, aneurysm location, and perioperative hypotension were significantly related with lowest mean CPP less than 65 mm Hg in univariate analysis (Supplementary Table 1, Supplemental Digital Content 1, http://links.lww.com/CCM/B83). In the multivariable model, only the neurologic status evaluated before aneurysm treatment and CT early lesion were significantly related with low CPP, whereas perioperative hypotension showed a relationship marginally significant (Supplementary Table 2, Supplemental Digital Content 1, http://links.lww.com/CCM/B83). Indicators of model performance showed $R^2 = 0.33$, goodness of fitness with $p = 0.14$ and $c = 0.77$. Lowest mean CPP showed significant relationship with mortality and unfavorable outcome in univariate analysis (Table 4) but not in the multivariable models.
TABLE 4. Univariate Analysis for Factors Related to 6-Month Mortality and Unfavorable Outcome

| Variable                              | Survivors | Deaths | p     | Favorable Outcome | Unfavorable Outcome | p     |
|---------------------------------------|-----------|--------|-------|-------------------|----------------------|-------|
| Age (mean ± sd)                       | 56±12     | 60±14  | 0.44  | 52±12             | 59±13                | 0.013 |
| Sex                                   | 0.039     |        |       |                   |                      |       |
| Female                                | 58        | 21     |       | 20                | 59                   |       |
| Male                                  | 15        | 14     |       | 7                 | 22                   |       |
| Fisher                                | 0.49      |        |       |                   |                      |       |
| 3                                     | 51        | 27     |       | 20                | 60                   |       |
| 2 and 4                               | 22        | 8      |       | 7                 | 21                   |       |
| Shift > 5 mm                          | 0.61      |        |       |                   |                      | 0.17  |
| Yes                                   | 17        | 6      |       | 3                 | 20                   |       |
| No                                    | 56        | 29     |       | 24                | 61                   |       |
| Intracerebral hematoma                | 0.86      |        |       |                   |                      | 0.07  |
| Yes                                   | 34        | 15     |       | 8                 | 41                   |       |
| No                                    | 39        | 20     |       | 19                | 40                   |       |
| Hydrocephalus                         | 0.53      |        |       |                   |                      | 0.82  |
| Yes                                   | 38        | 21     |       | 14                | 45                   |       |
| No                                    | 35        | 14     |       | 13                | 36                   |       |
| Aneurysm treatment                    | 0.33      |        |       |                   |                      | 0.79  |
| Coiling                               | 52        | 26     |       | 21                | 57                   |       |
| Clipping                              | 21        | 6      |       | 6                 | 21                   |       |
| Complication                          | 1         |        |       |                   |                      | 0.65  |
| Yes                                   | 38        | 17     |       | 13                | 42                   |       |
| No                                    | 35        | 15     |       | 14                | 36                   |       |
| Neurologic status before treatment    | 0.29      |        |       |                   |                      | 0.02  |
| Severe                                | 41        | 24     |       | 11                | 54                   |       |
| Mild                                  | 32        | 11     |       | 16                | 27                   |       |
| Neurologic status after treatment     | 0.052     |        |       |                   |                      | <0.001|
| Severe                                | 56        | 30     |       | 15                | 71                   |       |
| Mild                                  | 17        | 2      |       | 12                | 7                    |       |
| Rebleeding                            | 0.53      |        |       |                   |                      | 0.49  |
| Yes                                   | 28        | 16     |       | 9                 | 35                   |       |
| No                                    | 45        | 19     |       | 18                | 46                   |       |
| CT early lesion                       | 0.07      |        |       |                   |                      | 0.001 |
| Yes                                   | 48        | 29     |       | 12                | 65                   |       |
| No                                    | 25        | 6      |       | 15                | 16                   |       |

(Continued)
ICP and unfavorable outcome (pooling death, vegetative state, and severe disability). A possible interpretation is that important pathological events affecting brain integrity and function after SAH do not necessarily cause HICP. Regional hypoperfusion and ischemia, detected in microdialysis and perfusion studies (17, 18), may not be disclosed by a global monitor of increased intracranial volume like ICP.

Our findings confirm and extend results from two similar studies (5, 6). Heuer et al (5) reported daily highest mean ICP greater than 20 mm Hg in 54% of 433 surgically treated patients and a relationship between HICP, early severity, and mortality; Ryttlefors et al (6) reported episodes of HICP in 25% of 99 patients; HICP was associated with clinical deterioration but not with unfavorable outcome. Furthermore, our results seem to be in line with data from patients with traumatic brain injury (19, 20) and intracerebral hemorrhage (21, 22) that showed a strong relationship of high ICP with mortality but weaker with unfavorable functional outcome.

Our work has certain limitations. This was a single-center observational study in selected patients, so any generalization...
TABLE 5. Multivariable Model for 6-Month Unfavorable Outcome and Mortality

| Variable                          | OR (95% CI)          | p    |
|-----------------------------------|----------------------|------|
| **Unfavorable outcome**           |                      |      |
| Neurologic status after aneurysm treatment (severe vs mild) | 5.82 (1.56–21.73) | 0.008|
| CT lesion at any time             | 9.12 (2.09–39.7)    | 0.003|
| Age (per unit)                    | 1.07 (1.02–1.12)    | 0.002|
| Highest mean ICP (per mm Hg)      | 1.05 (0.99–1.12)    | 0.146|
| **Mortality**                     |                      |      |
| Highest mean ICP (per mm Hg)      | 1.08 (1.04–1.23)    | 0.001|

OR = odds ratio, ICP = intracranial pressure.

calls for caution. The majority of patients underwent ICP monitoring after clipping/coiling of the aneurysm, surgical removal of any large intracranial mass, EVD placement with CSF drainage, and so on. It is likely, therefore, that the real prevalence and severity of HICP, especially in the first hours after bleeding, was underestimated in our recordings. For the same reason, the real impact of hydrocephalus on HICP was probably mitigated. HICP was treated aggressively, so this investigation obviously does not represent the natural course of ICP after SAH.

In our center, studies about ICP waveform and cerebral autoregulation are not performed systematically, and we were unable to include these data in our analysis. Whether these variables had a relationship with HICP and outcome in patients with SAH could be the subject of future studies focusing on a limited number of patients (23).

Additionally, we focused our investigations on intracranial features and did not fully analyze systemic complications, such as fever, electrolyte imbalance, and cardiac and respiratory failure, which may affect ICP and outcome. The number of patients that developed cardiac failure or acute respiratory distress syndrome was too small to include these complications in the models. We tried to indirectly account them considering patients with hypotension and hypoxia, but no relationship was found.

Lacking a randomized control group, the study could not demonstrate the benefits of monitoring and treating ICP in patients with severe SAH. However, our findings indicate that HICP is frequent and plays an important role in the clinical course of SAH.

CONCLUSIONS

High ICP is a common complication in the first week after SAH in severe cases admitted to ICU. It is associated with severity of early brain injury and with mortality.

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