Effect of Cisternal and Ventricular Blood on Risk of Delayed Cerebral Ischemia After Subarachnoid Hemorrhage

The Fisher Scale Revisited

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Background and Purpose—Thick cisternal clot on CT is a well-recognized risk factor for delayed cerebral ischemia (DCI) after subarachnoid hemorrhage (SAH). Whether intraventricular hemorrhage (IVH) or intracerebral hemorrhage (ICH) predisposes to DCI is unclear. The Fisher CT grading scale identifies thick SAH but does not separately account for IVH or ICH.

Methods—We studied 276 consecutively admitted patients with an available admission CT scan performed within 72 hours of onset. Demographic, clinical, laboratory, and neuroimaging data were recorded, and the amount and location of SAH, IVH, and ICH on admission CT scans were quantified. The relationship between these variables and DCI was analyzed separately and in combination with multiple logistic regression.

Results—DCI developed in 20% of patients (54 of 276). Among SAH variables, thick clot completely filling any cistern or fissure was the best predictor of DCI ($P=0.008$), and among IVH variables, blood in both lateral ventricles was most predictive ($P=0.001$). These variables had independent predictive value for DCI in a multivariate analysis of CT findings, and both were included in a final multivariate model when evaluated in conjunction with other clinical risk factors: IVH (OR 4.1, 95% CI 1.7 to 9.8), SAH (OR 2.3, 95% CI 1.5 to 9.5), mean arterial pressure >112 mm Hg (OR 4.9, 95% CI 2.1 to 11.4), and transcranial Doppler mean velocity >140 cm/s within 5 days of hemorrhage (OR 3.8, 95% CI 1.5 to 9.5). Similar results were obtained in a repeat analysis with infarction due to vasospasm as the dependent variable.

Conclusions—SAH completely filling any cistern or fissure and IVH in the lateral ventricles are both risk factors for DCI, and their risk is additive. We propose a new SAH rating scale that accounts for the independent predictive value of subarachnoid and ventricular blood for DCI. **(*Stroke*. 2001;32:2012-2020.)**

Key Words: cerebral hemorrhage ■ cerebral infarction ■ cerebral ischemia ■ intracranial aneurysm ■ risk factors ■ subarachnoid hemorrhage

Delayed cerebral ischemia (DCI) from vasospasm is an important cause of complications and death after aneurysmal subarachnoid hemorrhage (SAH).[1,2] Breakdown products of blood, such as oxyhemoglobin, are considered to be the leading cause of vasospasm.[2,3] Angiographic vasospasm is detected in 50% to 70% of patients with SAH,[4] and DCI occurs in 19% to 46% of patients.[5–10]

Thick subarachnoid clot on admission CT has been associated with the development of DCI after SAH.[5–9,11–20] The Fisher CT grading scale,[21] which evaluates the amount of cisternal blood and the presence of intraventricular hemorrhage (IVH) or intracerebral hemorrhage (ICH), is widely used in the United States to identify patients at high risk for the development of DCI. Although the Fisher scale identifies patients with thick cisternal blood (grade 3), it does not differentiate between ICH and IVH (both grade 4), nor does it consider the potential for higher risk in patients with thick cisternal and ventricular or parenchymal blood. Two studies have found an association between IVH and DCI, but both found cisternal blood to be an even stronger predictor.[5,6]

In the present study, we separately assessed the amount and exact location of blood in the subarachnoid, intraventricular, and intracerebral compartments on the admission CT scan of patients with SAH. In a multivariate analyses, we identified significant independent CT predictors of DCI and then determined whether these CT variables retained their predictive value when considered in conjunction with other clinical risk factors. Our goal was to develop an easy-to-use CT rating scale with superior predictive value for DCI and infarction due to vasospasm.

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Subjects and Methods

Patient Population

Three hundred one patients with SAH consecutively admitted to the Neurological Intensive Care Unit (NICU) of Columbia-Presbyterian Medical Center between July 1996 and November 1999 were prospectively enrolled in the Columbia University SAH Outcomes Project. The study was approved by the hospital institutional review board, and in all cases, written informed consent was obtained from the patient or a surrogate.

The diagnosis of SAH was established on the basis of admission CT scans or by xanthochromia of the cerebrospinal fluid if the CT scan was negative. Patients with SAH from trauma or arteriovenous malformations were excluded, as were patients who were admitted ≥4 days after SAH onset. Because the earliest diagnosis of DCI (defined later) in our patient population was made on day 3 after onset, 9 patients who died within 2 days of the onset of symptoms were excluded from further analysis. In 16 additional cases, the admission CT scan was not available for formal rating, and these patients were also excluded.

For the remaining 276 patients, demographic data, social and past medical history, and clinical features at onset were obtained via patient and family interview shortly after admission. A neurological and general medical evaluation was performed by a study neurologist on admission. Clinical status on admission was assessed with the Glasgow Coma Scale (GCS), the National Institutes of Health Stroke Scale (NIHSS), the Hunt-Hess scale, and the Acute Physiology and Chronic Health Evaluation-2 (APACHE-2) scale. An APACHE-2 physiological subscore was calculated by subtracting the GCS, age, and chronic health elements from the APACHE -2 score. Admission (obtained within 72 hours of SAH) and all follow-up CT scans were independently evaluated by a study neurologist for the amount and location of blood, severity of hydrocephalus, and the presence of infarction (see later). Angiographic findings (within 4 days of onset) and transcranial Doppler (TCD) sonography results were also recorded. Outcome was assessed 3 months after SAH with the modified Rankin Scale via telephone or in-person interview of both the patient and a caregiver or family member.

Clinical Management

While the patient was in the NICU, TCD sonography was performed daily or every other day, and all patients received oral nimodipine. A ventricular catheter was placed in all patients with ventriculomegaly or IVH and decreased level of consciousness that could not be attributed to causes other than hydrocephalus. CT scanning was performed to evaluate all instances of clinical deterioration. All patients were administered 0.9% saline and supplemental 5% albumin solution to maintain central venous pressure at >8 mm Hg, and those with clinical deterioration from DCI were treated with hypertensive hypervolemic therapy (HHT) to maintain systolic blood pressure at >200 mm Hg. When significant clinical symptoms persisted despite HHT, balloon angioplasty of vasospastic vessels was performed, when feasible.

Definition of DCI

DCI was defined as otherwise unexplained (1) clinical deterioration (ie, a new focal deficit, decrease in level of consciousness, or both) or (2) a new infarct on CT that was not visible on the admission or immediate postoperative scan, or both. Other potential causes of clinical deterioration, such as hydrocephalus, rebleeding, or seizures, were rigorously excluded. DCI was diagnosed by the treating study neurologist and confirmed in a retrospective review of each subject's clinical course by 2 additional study physicians. Evidence of arterial spasm by TCD or angiography was generally used to support the diagnosis but was not mandatory.

Admission CT Risk Factors

The amount of SAH in 10 individual cisterns or fissures was quantified according to Hijdra et al[6]: 0 indicates no blood; 1, small SAH; 2, moderate SAH; and 3, completely filled with SAH. These scores were added to yield an SAH sum score that ranged from 0 to 30. The amount of IVH was quantified in both lateral, the third, and the fourth ventricles as follows[17]: 0 indicates no blood; 1, sedimentation (<25% filled); 2, moderately filled; and 3, completely filled, leading to an IVH sum score ranging from 0 to 12. Parenchymal ICH, when present, was evaluated by calculating the volume of the clot with the ABC/2 method.[22] Hydrocephalus was evaluated by measuring the bicaudate index and the temporal horn diameter.[23] Each scan was also evaluated with the 4-point Fisher scale[21]: 1 indicates none or minimal SAH; 2, diffuse thin SAH; 3, large clot or thick layer of SAH (exceeding 5 mm in thickness over the entire length of a cistern or fissure); and 4, diffuse thin or no SAH, with significant ICH or IVH. Because the Fisher scale does not separately quantify SAH, IVH, and ICH, it was not included in the multivariate analysis of DCI predictors. To assess the interobserver reliability of our CT measurements of SAH and IVH, we compared the scores of 2 independent blinded examiners in a convenience sample of 32 subjects.

Non-CT Risk Factors

Clinical variables tested for a possible association with DCI included demographic factors (age, sex, ethnicity, body mass index), social history (alcohol, smoking, cocaine use), past medical history (hypertension, diabetes mellitus, cardiac disease, stroke, headache), clinical and laboratory features at onset (sentinel bleeding, symptoms at SAH onset, mean arterial pressure [MAP] on admission, APACHE-2 physiological subscore), neurological examination on admission (GCS, NIHSS, Hunt-Hess scale), neuroimaging data (angiographic and TCD findings), and the method of aneurysm treatment (surgical clipping versus embolization). To evaluate the clinical relevance of DCI, we tested the association of DCI with NICU and hospital length of stay, hospital and 90-day mortality rates, and functional outcome among survivors at 3 months.

Statistical Analysis

Data analysis were performed with commercially available statistical software (SPSS version 9.0; SPSS Inc). Weighted κ (K_w) scores were calculated to assess the interobserver reliability of individual SAH and IVH sum scores, scores within individual cisterns and ventricles, and Fisher scale scores. The χ^2 test was used to identify dichotomized or categorical variables associated with the development of DCI. Continuous variables were dichotomized to evaluate categories that could be applied to a clinical scale: SAH and IVH sum scores and ICH volumes were dichotomized at the 25th, 50th, and 75th percentiles. We evaluated the number of cisterns or ventricles that had any blood (score ≥1), moderate blood (score ≥2), or complete filling with blood (score 3) and the presence of any blood (score ≥1) or complete filling with blood (score 3) in each individual cistern and ventricle. Bicaudate index and mean temporal horn diameter were also dichotomized at the 25th, 50th, and 75th percentiles; other continuous variables were dichotomized at the median. Comparison of mean length of stay was tested with independent-sample *t* tests (2-tailed). The association of 3-month modified Rankin Scale scores with DCI was tested with the Spearman test.

Independent predictors of DCI were identified in 4 steps with backward stepwise multiple logistic regression. Our goal was to identify SAH, IVH, and ICH variables with independent predictive value for DCI and infarction that might be applicable to a new CT rating scale. In step 1, independent predictors were separately identified among SAH, IVH, or ICH variables that showed a significant association with DCI in the univariate analysis. In step 2, a backward selection procedure was used to create a "combined CT" logistic regression model from the SAH, IVH, and ICH predictors identified in step 1 to evaluate their simultaneous effects. In step 3, we assessed the predictive value of alternative models by substituting different significant univariate SAH and IVH variables for those that were selected in the combined CT model. In step 4, clinical variables associated with DCI were added to the combined CT model to assess whether these CT variables retained their significance. Tests for interaction were performed for all variables entered into multivariable models. To estimate the predictive power of each model, the

TABLE 1. CT Predictors of DCI and Infarction: Subarachnoid Blood

Risk Factor	Criteria	Affected (n)	DCI* PPV, % (n)	DCI* OR	DCI* *P*	Infarction PPV, % (n)	Infarction OR	Infarction *P*
SAH sum score	≥8	201	20 (42)	1.4	0.494	13 (27)	1.5	0.418
	≥15	137	25 (34)	1.9	0.034†	17 (23)	2.3	0.029†‡
	≥21	68	24 (16)	1.4	0.380	21 (14)	2.4	0.032†
No. of cisterns with any blood (score ≥1)	≥1	258	21 (54)	NA	0.029†‡	13 (34)	NA	0.143
	≥3	229	21 (48)	1.8	0.308	14 (31)	2.2	0.227
	≥5	212	20 (43)	1.2	0.719	14 (28)	1.4	0.519
No. of moderately or completely filled	≥1	214	22 (47)	2.2	0.099	14 (31)	3.3	0.048†
cisterns (score ≥2)	≥3	161	24 (38)	1.9	0.064	15 (24)	1.8	0.141
	≥5	109	26 (28)	1.9	0.045†‡	17 (19)	2.1	0.060
No. of completely filled cisterns (score 3)	≥1	164	25 (41)	2.5	0.008†§	16 (27)	2.9	0.014†‡
	≥3	92	27 (25)	2.0	0.036†‡	20 (18)	2.5	0.018†‡
	≥5	51	27 (14)	1.7	0.123	24 (12)	2.8	0.016†
SAH scores in selected cisterns and fissures								
Anterior interhemispheric fissure	1–3	208	22 (45)	1.8	0.160	14 (29)	2.0	0.202
	3	37	32 (12)	2.2	0.045†	24 (9)	2.7	0.029†
Lateral sylvian fissure	1–3	213	21 (44)	1.4	0.474	13 (27)	1.1	1.00
	3	78	27 (21)	1.8	0.065	21 (16)	2.6	0.014†
Basal sylvian fissure	1–3	221	21 (47)	1.9	0.185	14 (30)	2.0	0.255
	3	88	28 (25)	2.2	0.015†‡	22 (19)	3.2	0.003†§
Suprasellar cistern	1–3	226	21 (48)	1.9	0.170	14 (32)	3.9	0.056
	3	113	25 (28)	1.7	0.090	18 (20)	2.3	0.039†

PPV indicates positive predictive value.

SAH scores were assessed in 10 cisterns and fissures: 0, no SAH; 1, small amount of SAH; 2, moderate amount of SAH; 3, completely filled with SAH. Sum scores were calculated by adding each of the 10 individual cistern scores (range 0–30). OR refers to risk of development of DCI or infarction in patients with risk factors compared with those without. Data are not shown for the ambient or quadrigeminal cisterns.

*Defined as clinical deterioration, infarction, or both.

†$P<0.05$.

‡Risk factors that remained in the "combined CT" logistic regression model when substituted for the risk factor labeled § (step 3).

§Risk factors that independently predicted DCI or infarction in the "combined CT" logistic regression model (step 2, refer to text for details).

correlation between the observed and predicted outcome was calculated for the combined CT (step 2) and CT plus clinical model (step 4). Jackknife versions of these correlations, which provide a better indication of model prediction based on resampling of the data,[24] were also calculated.

To confirm our results and to account for possible inaccuracy in the clinical diagnosis of DCI without infarction, we performed a repeat analysis with cerebral infarction as the main outcome variable. We used logistic regression to compare the overall predictive value of the Fisher scale and several possible new CT rating scales (constructed from risk factors identified in the multivariate analysis) for DCI and infarction. $P<0.05$ was considered significant.

Results

Baseline Information

Mean±SD age at the time of the hemorrhage was 54±15 years, and 178 patients (65%) were women. On admission, 70 patients (25%) were Hunt-Hess grade 1, 50 (18%) were grade 2, 93 (34%) were grade 3, 41 (15%) were grade 4, and 22(8%) were grade 5. IVH was seen in 53% of patients (146 of 276) on the admission CT scan; 23% had IVH in both lateral ventricles. In 30 patients (11%), no aneurysm was found on angiography, and in 9 patients (3%), angiography was not performed due to poor prognosis. Of the 237 patients with identified aneurysms, clipping was performed in 196 patients (83%), and embolization with Guglielmi detachable coils was performed in 37 patients (16%). An average of 3.6 CT scans were performed per patient (range 1 to 26 scans).

Clinical Features of DCI

Twenty percent of patients (54 of 276) developed DCI. Of these patients, clinical deterioration without infarction occurred in 20 patients (37%), clinical deterioration with infarction occurred in 21 patients (39%), and infarction alone occurred in 13 patients (24%). Angiographic vasospasm was present in all 30 patients studied with follow-up angiography. Symptomatic patients developed DCI an average of 7 days after SAH (range 3 to 15 days). Among the 20 patients who deteriorated clinically without infarction, 6 had a new focal deficit, 11 had a focal deficit with a change in mental status, and 3 had a change in mental status alone. All of these patients underwent CT scanning after deterioration. The average number of scans performed after deterioration was 2.7±1.9 (range 0 to 8 scans), and the average number of days between deterioration and the initial follow-up CT scan was 0.5±1.2 days; the initial scan was performed on the day deterioration occurred in 16 of 20 cases. Among patients with

TABLE 2. CT Predictors of DCI and Infarction: IVH

Risk Factor	Criteria	Affected (n)	DCI* PPV, % (n)	DCI* OR	DCI* *P*	Infarction PPV, % (n)	Infarction OR	Infarction *P*
IVH sum score	≥2	127	28 (35)	2.6	0.002†‡	20 (25)	3.8	0.001†‡
	≥3	79	29 (23)	2.2	0.018†‡	22 (17)	2.9	0.007†‡
No. of ventricles with any blood	≥1	146	26 (38)	2.5	0.006†‡	18 (26)	3.3	0.005†‡
(score ≥1)	≥2	96	28 (27)	2.2	0.011†‡	23 (20)	3.1	0.003†‡
	≥3	58	31 (18)	2.3	0.024†‡	22 (13)	3.0	0.013†‡
No. of moderately or completely	≥1	94	26 (24)	1.7	0.081	21 (20)	3.2	0.002†‡
filled ventricles (score ≥2)	≥2	42	24 (10)	1.3	0.526	21 (9)	2.3	0.071
	≥3	24	21 (5)	1.1	0.794	17 (4)	1.5	0.515
IVH scores in individual ventricles								
Lateral ventricle	1–3	85	31 (26)	2.6	0.003†‡	21 (18)	2.9	0.005†‡
	3	14	21 (3)	1.1	0.742	21 (3)	2.0	0.393
Bilateral ventricles	1–3	63	35 (22)	3.0	0.001†§	24 (15)	3.2	0.004†§
	3	2	0 (0)	NA	1.00	0 (0)	NA	1.00
Third ventricle	1–3	73	25 (18)	1.5	0.230	22 (16)	2.9	0.006†‡
	3	18	11 (2)	0.5	0.540	11 (2)	0.9	1.00
Fourth ventricle	1–3	117	24 (28)	1.6	0.128	17 (20)	2.1	0.044†‡
	3	28	21 (6)	1.1	0.803	14 (4)	1.2	0.761

PPV indicates positive predictive value.

IVH scores (0–3) were assessed in each lateral, third and fourth ventricle: 0, no IVH; 1, intraventricular sedimentation (<25%); 2, partly filled ventricle; 3, completely filled ventricle. For IVH sum scores (range 0–12), all 4 ventricular blood scores were added. OR refers to risk of development of DCI or infarction in patients with risk factors compared to those without. Data are not shown for the number of completely filled ventricles (score 3).

*Defined as clinical deterioration, infarction, or both.

†$P<0.05$.

‡Risk factors that remained in the "combined CT" logistic regression model when substituted for the risk factor labeled § (step 3).

§Risk factors that independently predicted DCI or infarction in the "combined CT" logistic regression model (step 2, refer to text for details).

clinical deterioration, angioplasty was performed in 29% (12 of 41).

CT Reliability Testing

Interobserver reliability for our SAH and IVH measurements indicated good (K_w 0.6 to 0.8) to excellent (K_w 0.8 to 1.0) agreement. K_w was 0.54 to 0.75 for the individual SAH cistern scores, 0.61 for the SAH sum score, 0.71 to 0.86 for the individual IVH scores, 0.83 for the IVH sum score, 0.83 for the presence of ICH, and 0.86 for the Fisher scale.

Univariate Analysis

CT Variables

Five SAH (Table 1) and 7 IVH (Table 2) variables were associated with both DCI and infarction in the univariate analysis. None of the Fisher score, ICH, or hydrocephalus variables were associated with DCI; however, ICH and Fisher grade 4 were associated with infarction, whereas Fisher grade 1 was protective against infarction (Table 3)

Non-CT Variables

Five clinical variables were found to be related with both DCI and infarction: smoking within the previous 6 months, elevated blood pressure on admission (MAP >112 mm Hg), neurological deficits on admission (GSC score <15, NIHSS ≥6), and TCD velocities >140 cm/s within 5 days of hemorrhage (Table 4).

Multivariable Models to Predict DCI and Infarction

Step 1

Among SAH variables associated with DCI in the univariate analysis, only complete filling of any cistern or fissure remained in the SAH model (OR 2.5, 95% CI 1.3 to 4.9). Among SAH variables associated with infarction, only complete filling of the basal sylvian fissure remained in the SAH model (OR 3.1, 95% CT 1.5 to 6.5). Among IVH variables associated with DCI in the univariate analysis, only IVH in both lateral ventricles remained in the IVH model (OR 3.0, 95% CI 1.6 to 5.7). Among IVH variables associated with infarction, IVH in both lateral ventricles (OR 2.2, 95% CI 1.0 to 5.0) and moderate or complete filling of ≥1 ventricle (OR 2.4, 95% CI 1.1 to 5.4) remained in the IVH model. Among the ICH variables associated with infarction, the presence of ICH remained in the predictive model (OR 3.2, 95% CI 1.5 to 7.2).

Step 2

For predictors of DCI, both of the variables identified by logistic regression in step 1 were retained in a combined CT model when entered together (bilateral IVH, OR 2.7, 95% CI 1.4 to 5.1; complete filling of any cistern, OR 2.2, 95% CI 1.1 to 4.3; $P=0.0003$ for the entire model). The correlation of the observed outcome with the predicted outcome was 0.25, and the jackknife correlation was also 0.25. For predictors of infarction, 3 of the 4 variables identified by logistic regres-

TABLE 3. CT Predictors of DCI and Infarction: Other Variables

Risk Factor	Criteria	Affected (n)	DCI* PPV, % (n)	DCI* OR	DCI* *P*	Infarction PPV, % (n)	Infarction OR	Infarction *P*
Fisher CT score‖	1	50	10 (5)	0.4	0.075	2 (1)	0.1	0.015†
	2	85	14 (12)	0.6	0.142	8 (7)	0.5	0.233
	3	70	27 (19)	1.8	0.081	17 (12)	1.7	0.205
	4	71	25 (18)	1.6	0.167	20 (14)	2.3	0.036†
ICH present		51	27 (14)	1.8	0.121	25 (13)	3.3	0.004†§
ICH volume, mL	≥5	30	27 (8)	1.6	0.332	27 (8)	3.0	0.019†
	≥10	21	33 (7)	2.2	0.148	33 (7)	4.2	0.008†‡
	≥20	12	33 (4)	2.1	0.261	33 (4)	3.9	0.048†

PPV indicates positive predictive value.

OR refers to risk of development of DCI or infarction in patients with risk factors compared with those without.

*Defined as clinical deterioration, infarction, or both.

†$P<0.05$.

‡Risk factor that remained in the "combined CT" logistic regression model when substituted for the risk factor labeled § (step 3).

§Risk factor that independently predicted infarction in the "combined CT" logistic regression model (step 2, refer to text for details).

‖Fisher CT score: 1, no SAH; 2, diffuse thin SAH; 3, clot or thick layer of SAH; 4, ICH or IVH with no or diffuse SAH.

sion in step 1 were retained in a combined CT model when entered together (bilateral IVH, OR 2.7, 95% CI 1.2 to 5.81; complete filling of the basal sylvian fissure: OR 2.4, 95% CI 1.1 to 5.2; ICH present, OR 2.4, 95% CI 1.0 to 5.4; $P=0.0001$ for the entire model). The correlation of the observed outcome with the predicted outcome was 0.28, and the jackknife correlation was 0.26. None of the other SAH or IVH variables associated with DCI or infarction in the univariate analysis added further predictive value when sequentially entered into these models, and no interactions between variables in these models were found.

Step 3

When other SAH variables associated with DCI in the univariate analysis were substituted for complete filling of any cistern in the combined CT model for DCI, 4 stayed in the model when evaluated with the strongest IVH predictor, bilateral ventricular hemorrhage (Table 1). When SAH variables associated with infarction were substituted for complete filling of the basal sylvian fissure in the combined CT model for infarction, 3 were retained when evaluated with bilateral IVH and the presence of ICH (Table 1). All IVH predictors identified in the univariate analysis were retained in the combined CT models for DCI and infarction when substituted for bilateral IVH.

Step 4

The CT plus clinical model for DCI identified 4 independent predictors: MAP >112 mm Hg (OR 4.9, 95% CI 2.1 to 11.4), IVH in both lateral ventricles (OR 4.1, 95% CI 1.7 to 9.8), mean TCD velocities >140 cm/s within 5 days of SAH (OR 3.8, 95% CI 1.5 to 9.5), and thick SAH in any cistern or fissure (OR 2.3, 95% CI 1.5 to 9.5). The correlation of the observed outcome with the predicted outcome was 0.35, and the corresponding jackknife correlation was 0.33. The CT plus clinical model for infarction identified 6 independent predictors: mean TCD velocities >140 cm/s within 5 days of SAH (OR 3.6, 95% CI 1.3 to 9.5), GCS <15 (OR 3.0, 95%

TABLE 4. Non-CT Predictors of DCI and Infarction

Risk Factor	Affected (n)	DCI* PPV, % (n)	DCI* OR	DCI* *P*	Infarction PPV, % (n)	Infarction OR	Infarction *P*
Smoking currently§	112	22 (25)	1.6	0.231	17 (19)	2.7	0.039†
Smoking within 6 mo	121	27 (33)	2.4	0.006†	19 (23)	3.1	0.003†‡
Admission MAP >112 mm Hg	139	28 (39)	3.3	0.000†‡	17 (23)	2.5	0.026†‡
Admission GCS <15	143	26 (37)	2.4	0.006†	19 (27)	4.2	0.001†‡
Admission NIHSS ≥6	72	31 (22)	2.4	0.009†	28 (20)	5.2	0.000†
Admission Hunt and Hess grade ≥3	156	23 (36)	1.7	0.152	17 (27)	3.4	0.005†
TCD >140 within 5 d of SAH	37	38 (14)	2.7	0.015†‡	27 (10)	3.1	0.014†‡

PPV indicates positive predictive value.

*Defined as clinical deterioration, infarction, or both.

†$P<0.05$.

‡Risk factors that remained in the "CT plus clinical" logistic regression model (step 4).

§Any cigarettes within 7 d of admission.

TABLE 5. Proposed SAH CT Rating Scale

Grade	Criteria	Patients, %	Frequency, % (n) DCI	Frequency, % (n) Infarction
0	No SAH or IVH	5	0 (0/15)	0 (0/15)
1	Minimal/thin SAH, no IVH in both lateral ventricles	30	12 (10/83)	6 (5/83)
2	Minimal/thin SAH, *with* IVH in both lateral ventricles	5	21 (3/14)	14 (2/14)
3	Thick SAH,* no IVH in both lateral ventricles	43	19 (22/117)	12 (14/117)
4	Thick SAH,* *with* IVH in both lateral ventricles	17	40 (19/47)	28 (13/47)
All patients		100	20 (54/276)	12 (34/276)

*Completely filling ≥1 cistern or fissure.

CI 1.0 to 9.1), smoking within 6 months of SAH (OR 2.8, 95% 1.1 to 6.7), bilateral IVH (OR 2.7, 95% CI 1.1 to 6.8), complete filling in any cistern or fissure (OR 2.6, 95% CI 1.1 to 6.1), and MAP >112 mm Hg (OR 2.4, 95% CI 1.0 to 6.1). The correlation of the observed outcome with the predicted outcome was 0.42, and the corresponding jackknife correlation was 0.38. Both models reached a significance level of $P<0.0001$. Two-way interaction terms were calculated for all variables that were entered in the final models. The only significant interaction we found was between smoking and complete filling of any cistern or fissure in the model predicting infarction: complete filling of any cistern or fissure was predictive of infarction among nonsmokers (OR 17.1, 95% CI 2.0 to 149.0) but not among smokers (OR 1.3, 95% CI 0.01 to 98.2).

Evaluation of New CT Rating Scales

We constructed 6 potential SAH CT rating scales by combining variables that were equivalently predictive of both DCI and infarction in the combined CT models and were reasonable to apply to a clinical scale. We used complete filling of ≥1 cistern or fissure as the SAH variable, and we compared unilateral, bilateral, and any IVH, either alone or with ICH, as the secondary variable. Table 5 shows the model that had the highest predictive and discriminatory value between levels for DCI (OR 1.7, 95% CI 1.3 to 2.3, $P=0.0003$) and infarction (OR 1.8, 95% CI 1.3 to 2.7, $P=0.0012$) when evaluated with logistic regression. The new scale classifies no SAH or IVH (grade 0) on the admission CT as very low risk, minimal or diffuse thin SAH without bilateral IVH (grade 1) as low risk, minimal or thin SAH with bilateral IVH (grade 2) and SAH completely filling any cistern or fissure without bilateral IVH (grade 3) as intermediate risk, and SAH completely filling any cistern or fissure with bilateral IVH (grade 4) as high risk (Figure). Mean SAH sum scores did not differ between grades 1 and 2 (8 ± 6 versus 8 ± 4, respectively; $P=0.84$) or between grades 3 and 4 (19 ± 6 versus 20 ± 7, respectively; $P=0.43$).

The new CT rating scale was superior to the Fisher Scale for differentiation between different levels of risk for DCI ($P=0.0001$ versus $P=0.01$, logistic regression) as well as infarction ($P=0.0003$ versus $P=0.0015$, logistic regression).

Outcome

DCI was associated with increased NICU (mean 13.4 versus 8.8 days, $P<0.001$) and hospital (mean 25.3 versus 17.2 days, $P=0.001$) length of stay. Neither hospital mortality (13% versus 10%, $P=0.63$) or 3-month mortality (15% versus 13%, $P=0.82$) rates were related to DCI. However, among surviving patients, worse 3-month outcome on the modified Rankin Scale was associated with DCI ($P=0.018$, Spearman's test).

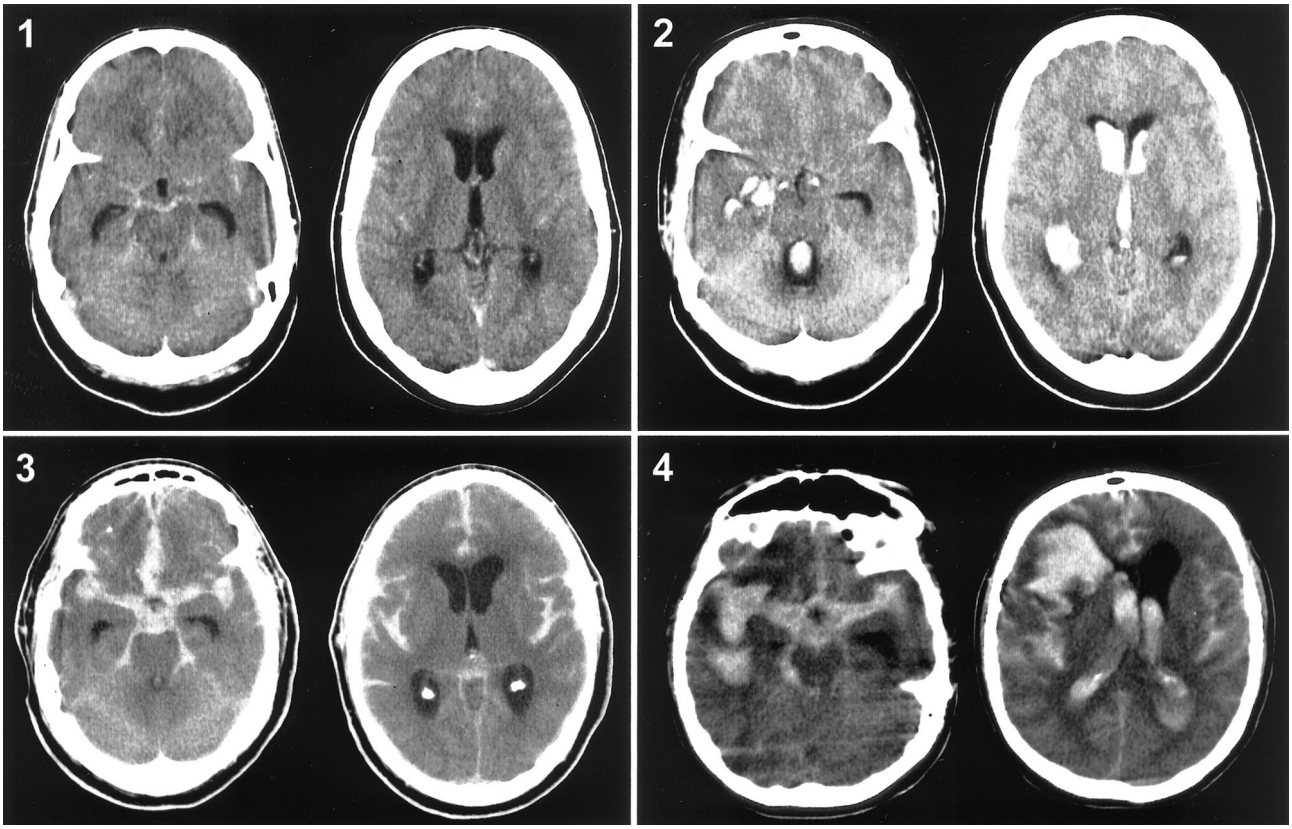
Discussion

In the present study, bilateral IVH and subarachnoid blood completely filling any cistern or fissure were important risk factors for DCI, and their risk was additive. When considered in the context of other clinical risk factors for DCI, both of these variables were retained in a final regression model, along with 2 other clinical variables: elevated MAP on admission and mean TCD velocities exceeding 140 cm/s within 5 days of onset. Moreover, nearly identical results were obtained when the analysis was limited to infarction alone. On the basis of these results, we propose a new SAH CT rating scale that accounts for the increased risk of DCI that occurs when blood extends into both lateral ventricles and completely fills ≥1 of the basal cisterns.

We included both good and poor clinical grade patients in our study, with Hunt-Hess scores similar to those of other large hospital-based series.[6,8] DCI occurred in 20% of our cohort, which is on the low end of previously published frequencies ranging from 19% to 46%.[5–10] The low frequency of DCI in our study may be explained in part by our aggressive use of HHT and angioplasty and by the fact that DCI was diagnosed only after careful exclusion of other possible causes of deterioration in a retrospective review of the patient's clinical course.

Among SAH variables, blood completely filling any cistern was identified as the strongest independent predictor of DCI. Although infarction was best predicted by complete filling of the basal sylvian fissure, which likely reflects the anatomic proximity of this location to the middle cerebral artery, complete filling of any cistern was found to be of equivalent predictive value. In contrast, SAH sum score cutoffs were less predictive of DCI. Others have suggested that the overall quantity of subarachnoid blood is the most important risk factor,[18] but our results confirm the notion proposed by Fisher et al[21] and Kistler et al[11] that thick focal clot in specific locations (ie, the basal cisterns) best predicts DCI.

Bilateral IVH was identified as the strongest independent predictor of both DCI and infarction among the IVH variables we studied. However, many other IVH variables, including varying IVH sum score cutoffs and IVH within 1, 2, or 3



Proposed SAH CT rating scale: grade 1 (minimal or diffuse thin SAH without bilateral IVH), indicating low risk for DCI; grade 2 (minimal or thin SAH with bilateral IVH) and grade 3 (cisternal clot without bilateral IVH), indicating intermediate risk for DCI; and grade 4 (cisternal clot with bilateral IVH), indicating high risk for DCI.

ventricles, had equivalent predictive value when considered in conjunction with thick cisternal SAH. These results suggest that although the presence of any ventricular blood predisposes to DCI, the risk is highest when blood is present in both lateral ventricles. This may reflect a larger overall extent of IVH when blood is in both lateral ventricles or closer proximity of blood in this location to the deep cortical vascular territories.

The association of large amounts of cisternal subarachnoid blood with angiographic and TCD evidence of arterial spasm,[8,11,16,19] and with symptomatic vasospasm,[5–9,12–18,20] is well described. Whether IVH or ICH also predisposes to DCI has been less clear. Four studies have separately assessed IVH and SAH as risk factors for deterioration or infarction from vasospasm,[5,6,12,17] with conflicting results: 2 found a relationship between IVH and DCI,[5,6] and 2 others did not.[12,17] In a study of 176 patients, Hijdra et al[6] found that the amount of SAH and IVH, and treatment with tranexamic acid, were independently predictive in a multivariate model. In a study of 283 patients, Qureshi et al[5] found a univariate association between IVH and DCI, but IVH did not remain in the final multivariate model. Although ICH was predictive of infarction in our study, this relationship was not significant when both CT and clinical variables were considered, and we failed to find an association with DCI, as have others.[5,12,17] Several investigators have identified acute hydrocephalus as a risk factor for symptomatic vasospasm,[6,23] but others have not.[5,12] Ventricular size was not predictive of DCI in our study, suggesting that the risk of delayed ischemia is more related to the amount of ventricular blood than to the extent of CSF obstruction.

The mechanism by which IVH may increase susceptibility to DCI is unknown. Several case reports have demonstrated that IVH related to ruptured arteriovenous malformations can result in symptomatic vasospasm of the proximal cerebral arteries in the absence of SAH.[25–27] All of these cases occurred in young women, and the mechanism for this phenomenon is unknown. Although it is possible that IVH may promote proximal arterial spasm, adverse effects on cerebral blood flow or tissue tolerance for ischemia may also increase susceptibility to DCI. IVH in dogs has been shown to cause periventricular blood infiltration, extensive ependymal disruption, cellular desquamation, and subependymal gliosis involving the ventricular walls.[28,29] Injury of this type in brain regions adjacent to ventricular blood may exacerbate ischemia or adversely affect the cerebral microcirculation. Because all of our patients with acute hydrocephalus and depressed level of consciousness were treated with ventricular drainage, it is unlikely that reduced cerebral perfusion pressure related to elevated intracranial pressure can explain why IVH predisposed to DCI.

In their seminal study, Fisher et al[21] did not emphasize ICH and IVH as risk factors for DCI. Fisher's scale does not distinguish between IVH and ICH and does not differentiate patients with thick cisternal clot and IVH from those without IVH. Other proposed CT rating scales for SAH have ignored

IVH and ICH altogether.[18–20] To account for the independent predictive value of IVH for DCI, we have proposed a new scale (Table 5), which in our patient population was superior to the Fisher scale for differentiation of patients at low, intermediate, and high risk. After considering all SAH and IVH variables with equivalent predictive value in our combined CT model (step 3), we chose 2 criteria (SAH that completely fills 1 cistern or fissure, and IVH in both lateral ventricles) because of their ease of interpretation and superior predictive value. Importantly, the criterion applied to identify "thick" cisternal blood in the new scale, which was adapted from the Hijdra CT rating scale,[6] was less stringent and hence more widely applied than the criterion we used to define a Fisher grade of 3 (SAH of ≥5-mm thickness extending for the entire length of a cistern or fissure). Additional studies are needed to confirm that our new scale better discriminates between different levels of risk for DCI than the Fisher scale.

Our study has several limitations. Interobserver variability in grading the amount of blood may hamper the usefulness of the CT rating scales in general[30,31] and may have affected the accuracy of our SAH scores. The fact that our SAH measurements were slightly less reliable than those for IVH may explain why SAH sum scores were not predictive of DCI in our univariate analysis and why IVH was a stronger predictor of DCI than SAH in the multivariable models. More specific criteria for different category levels may lead to improved agreement for CT rating scales in the future[31]; we intend to prospectively assess the reliability of our new scale in a future analysis. Varying definitions and observer bias may also affect the accuracy of diagnosing DCI,[32] and this limitation may hamper comparisons between different studies. In contrast to others, we included asymptomatic infarction in our definition of DCI[33] and did not require documentation of arterial spasm by TCD (because of its high false-negative rate) or angiography (if it was not performed). Finally, the same study neurologist who performed the CT rating on admission was later responsible for the diagnosis of DCI, which may have introduced bias. To improve diagnostic accuracy, the designation of DCI in our study was independently confirmed by 2 additional study physicians. To compensate for these limitations, we repeated our analysis with cerebral infarction as the main outcome variable, to confirm our analysis of DCI predictors with a more reliable but less inclusive outcome measure.

In conclusion, our findings indicate that both cisternal and ventricular blood are risk factors for DCI after SAH. Further research is needed to explain how intraventricular blood predisposes to ischemic injury, to confirm that our proposed SAH CT rating scale has superior predictive value for DCI compared with the Fisher scale, and to develop treatments to ameliorate the negative impact that IVH has on outcome after SAH.

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Effect of Cisternal and Ventricular Blood on Risk of Delayed Cerebral Ischemia After Subarachnoid Hemorrhage:: The Fisher Scale Revisited

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