Regional Myocardial Perfusion After Experimental Subarachnoid Hemorrhage

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Background and Purpose—The pathophysiology of cardiac injury after subarachnoid hemorrhage (SAH) remains controversial. Data from animal models suggest that catecholamine-mediated injury is the most likely cause of cardiac injury after SAH. However, researchers also have proposed myocardial ischemia to be the underlying cause, as a result of coronary artery disease, coronary artery spasm, or hypertension and tachycardia. To test the hypothesis that SAH-induced cardiac injury occurs in the absence of myocardial hypoperfusion, we developed an experimental canine model that reproduces the clinical and pathological cardiac lesions of SAH and defines the epicardial and microvascular coronary circulation.

Methods—Serial ECG, hemodynamic measurements, coronary angiography, regional myocardial blood flow measurements by radiolabeled microspheres, 2D echocardiography, and myocardial contrast echocardiography were performed in 9 dogs with experimental SAH and 5 controls.

Results—Regional wall motion abnormalities were identified in 8 of 9 SAH dogs and 1 of 5 controls (Fisher’s Exact Test, P = 0.02) but no evidence was seen of coronary artery disease or spasm by coronary angiography and of significant myocardial hypoperfusion by either regional myocardial blood flow or myocardial contrast echocardiography.

Conclusions—In this experimental model of SAH, a unique form of regional left ventricular dysfunction occurs in the absence of myocardial hypoperfusion. Future studies are justified to determine the cause of cardiac injury after SAH. (Stroke. 2000;31:1136-1143.)

Key Words: angiography ■ cerebrovascular disorders ■ echocardiography ■ regional blood flow ■ dogs

The association between central nervous system disease and cardiac dysfunction is well known and has been described in intracerebral hemorrhage, intracranial tumors, meningitis, and stroke.1 However, this association is particularly strong in subarachnoid hemorrhage (SAH),2 after which ECG changes,3,4 arrhythmia,5 left ventricular (LV) dysfunction,6,7 and elevations of the CPK (creatine phosphokinase)–MB fraction8,9 have been reported. Solenski et al10 have quantified the significant effect of cardiac injury on clinical outcomes in patients with SAH. In a prospective study of 457 SAH patients, these investigators reported a 5% risk of life-threatening cardiac arrhythmias, a 6% incidence of severe pulmonary edema, and a 4% incidence of cardiac failure.10

The pathophysiology of cardiac dysfunction after SAH in humans remains unknown and controversial. Although data from animal models indicates that catecholamine-mediated injury is the most likely cause of cardiac injury after SAH,2 some authors have implicated myocardial ischemia due to coronary artery disease,11 coronary vasospasm,12 or hypertension and tachycardia. In clinical practice, LV dysfunction after SAH is frequently ascribed to myocardial infarction.

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This controversy persists, in part, because of the lack of previous experimental studies of the epicardial and microvascular coronary circulation after SAH.

To test the hypothesis that SAH-induced cardiac injury occurs in the absence of myocardial hypoperfusion, we developed an experimental canine model that reproduces the clinical and pathological cardiac lesions of SAH and defines the epicardial and microvascular coronary circulation.

Materials and Methods

Animal Preparation
With approval by the Massachusetts General Hospital Subcommittee on Research Animal Care, an open-chest canine model was developed for the experiment. Each mongrel dog was weighed, and anesthesia was initiated with thiopental sodium (30 mg/kg IV, Abbott Laboratories) and maintained with isoflurane (1% to 2% inhalation, Fort Dodge Animal Health). Additional thiopental was administered during the experiment as needed. After dogs were intubated and given mechanical ventilation, ECG leads were placed on the dogs to monitor the limb and augmented leads. A heating pad...
was used to preventing hypothermia. An 8F catheter was placed in the left femoral artery to record arterial pressure and allow withdrawal of blood samples. A second 8F catheter was placed in the left femoral vein, and intravenous fluids were administered to maintain a left atrial pressure of 4 to 8 mm Hg. An 8F introducer (Arrow International) was placed in the right femoral vein, through which a 7.5F Swan-Ganz catheter (Baxter) was advanced to a distal pulmonary artery with hemodynamic and fluoroscopic guidance. This catheter was used to measure pulmonary arterial pressure and cardiac output by the thermodilution method.

A right lateral thoracotomy was performed, and the heart was suspended in a pericardial cradle. A 5F catheter was placed in the left atrium through a right pulmonary vein to measure left atrial pressure and inject radiolabeled microspheres. The femoral artery, pulmonary artery, and left atrial pressures were recorded on a polygraph (Hewlett Packard). An additional 5F catheter was placed in the aortic root by direct puncture for injection of angiography dye and ultrasound contrast agents. All catheters were flushed frequently with heparinized saline.

**Baseline Evaluation**

After surgery, an ECG was recorded and baseline hemodynamic parameters, including heart rate, arterial blood pressure, pulmonary artery pressure, left atrial pressure, and thermodilution cardiac output, were measured. A blood sample was withdrawn for measurement of total CPK-MB fraction (fluorometric enzyme immunoassay, Dade).

Coronary angiography was performed in a minimum of 2 projections with manual injections of 10 cm³ of radiographic contrast dye (Hexabrix, Mallinckrodt Medical) into the aortic root. Images were obtained with a portable fluoroscope connected to a video recorder and stored on videotape.

Two-dimensional echocardiographic scanning of regional LV function was performed with a phased-array system (Sonos 2500 LE, Hewlett Packard) with a 5-MHz probe placed on the epicardial surface of the right ventricle. Position of the probe was manually adjusted to obtain a short-axis view of the LV at the midpapillary level, and the gain and compression settings were optimized for visualization of the endocardial borders. Images were recorded on videotape.

**Myocardial Contrast Echocardiography**

Myocardial contrast echocardiography (MCE) was performed with the echocardiography system described above, but also with a transducer system capable of harmonic imaging (1.8-MHz transmit/3.6-MHz receive, Hewlett-Packard) to improve system sensitivity to ultrasound contrast agents. A ring stand and clamp were used to fix the probe in position on the epicardial surface of the right ventricle with hemodynamic and fluoroscopic guidance. This catheter was used to measure pulmonary arterial pressure and cardiac output by the thermodilution method.

**Myocardial Blood Flow Measurements**

Approximately 1- to 2×10⁶ 15-μm radiolabeled microspheres (Ce⁺⁺, Sn⁴⁺, Ru⁶⁺, Nb⁶⁺, or Sc⁵⁺, DuPont NEN) suspended in 3 mL of 0.9% saline solution/0.01% Tween 80 were injected during 5 seconds into the left atrium and flushed with 15 mL of warmed normal saline. For 3 minutes after the injection of microspheres, an arterial reference sample was withdrawn from the aortic root catheter with a constant-rate withdrawal pump. Different isotopes were used at the different time points in each experiment.

**Induction of SAH**

After baseline testing was completed, pre-SAH evaluation of ECG and hemodynamic measurements was performed. Immediately after these measurements were taken, each dog was randomized by blinded selection of a card-labeled SAH (n=9) or control (n=5) at an intentional 2:1 proportion.

In SAH dogs, a modified version of a previously validated technique was used to inject blood into the subarachnoid space. Each dog was placed in a 30° Trendelenberg position, and the neck was maximally flexed. A 19-gauge needle connected to extension tubing and a 3-way stopcock was inserted into the cisterna magna. After backflow of cerebrospinal fluid was seen, 0.4 mL/kg of autologous femoral arterial blood was injected during 2 minutes, followed by 1 mL (1000 U) of thrombin (Parke-Davis). Thrombin was injected with the blood to facilitate rapid clotting and accelerate the development of cardiac injury. ECG and blood pressure were continuously monitored at the time of SAH. After injection, dogs were kept in the Trendelenberg position for 30 minutes, with the neck turned toward midline to allow the blood to clot in the basal cistern. In control dogs, no injection was made into the cisterna magna, but the animals were placed in the Trendelenberg position for 30 minutes.

**Post-SAH Measurements**

After the 30-minute period in the Trendelenberg position, dogs were leveled and anticoagulated with 3000 to 4000 U of intravenous heparin to prevent thrombus formation on the intravascular catheters. ECG and hemodynamic measurements were repeated every 30 minutes after SAH, and 2D echocardiography was repeated every 60 minutes to evaluate regional wall motion abnormalities (RWMA) of the LV.

To determine whether an early or transient reduction in MBF occurred after SAH, MCE was performed and radiolabeled microspheres were injected in 6 dogs at 30 and 60 minutes after induction of SAH.

At either 4 (n=2 dogs) or 6 (n=12 dogs) hours after SAH, all baseline measurements were repeated, including ECG, hemodynamic measurements, CPK-MB fraction, coronary angiography, 2D echocardiography, MCE, and injection of radiolabeled microspheres. Euthanatization was then performed on each dog by intravenous injection of potassium chloride after additional thiopental dosing.

After euthanatization of the dogs, each heart was removed and a 1-cm-thick short-axis slice of the LV at the midpapillary level was resected, corresponding to the 2D echocardiogram and MCE view. This slice was sectioned into 16 pieces, which included the subendocardial and subepicardial layers of the anterior, anterolateral, posterolateral, posterior, inferior, inferoseptal, midseptal, and anteroseptal segments. These 16 LV pieces were placed in tubes, and their radioactivity was measured in a well counter with a multichannel analyzer (1282 Compugamma universal gamma counter, LKB Wallac). A custom-designed computer program was used to compensate for spectral overlap between the isotopes and generate corrected counts per minute.

The remainder of the heart was preserved in formalin for pathological examination. The slice of LV myocardium immediately superior to the slice taken to count radiolabeled microspheres was resected for light-microscopic evaluation. A minimum of 16 sections were obtained from the midpapillary level of the LV of each dog, and these were stained with hematoxylin and eosin and Masson’s trichrome. Foci of contraction-band necrosis (CBN) were identified.
on the sections by a cardiac pathologist (H.T.A.) who was blinded to the experimental status of each dog (SAH versus control). Gross examination of the brain was performed in the first 5 SAH animals to confirm the presence of blood clots in the subarachnoid space.

**Statistical Analysis**

Five hemodynamic variables (heart rate, systolic blood pressure, mean left atrial pressure, pulmonary artery pressure, and cardiac output) were assessed for differences between baseline and post-SAH measurements. Each variable was plotted against time, and the slopes of the regression lines were tested for significant differences from zero, indicating a change from baseline measurements.

All experimental ECGs were reviewed to determine whether new ST depression (≥1 mm), ST elevation (≥1 mm), or T-wave inversion occurred in comparison to pre-SAH ECGs for each dog. The proportion of dogs in the SAH and control groups with ECG changes was compared by Fisher’s Exact Test.

Baseline and post-SAH serum CPK-MB was measured in all dogs and was considered elevated if >5 ng/mL, with an index of >2.5%. The proportion of dogs in the SAH and control groups with elevations of CPK-MB fraction was compared by Fisher’s Exact Test.

Coronary angiograms were reviewed by a blinded observer for evidence of coronary artery disease or focal epicardial coronary spasm.

The 2D echo data were analyzed off-line by a blinded echocardiographer. Images from each dog at each stage were compiled in the experimental status of each dog (SAH versus control). Gross examination of the brain was performed in the first 5 SAH animals to confirm the presence of blood clots in the subarachnoid space. Five hemodynamic variables (heart rate, systolic blood pressure, mean left atrial pressure, mean pulmonary artery pressure, and cardiac output) were assessed for differences between baseline and post-SAH time points by repeated measures ANOVA.

Radiolabeled-microsphere determination of regional MBF (RMBF) was performed using the method of Heymann et al. Segmental/global MBF and subendocardial/subepicardial ratios were assessed at baseline and post-SAH time points by repeated measures ANOVA.

The proportions of dogs in SAH and control groups with CBN were compared with Fisher’s Exact Test. The correlation between RWMA and CBN was determined by Fisher’s Z test.

For all the above analyses, P<0.05 was considered statistically significant. Except as noted below, all data are expressed as mean±SD.

**Results**

The study included 9 SAH dogs and 5 controls. Average weights were 23.6±3.7 kg in the SAH group and 24.8±3.0 kg in the control group (t test, P=0.51). Hemodynamic data are shown in Table 1. During the 6-hour observation period, increases in heart rate (P=0.04) and pulmonary artery pressure (P=0.0001) were seen in the SAH group and a decrease in systolic blood pressure was seen in the control group (P=0.01). One SAH dog died before completion of the experiment (5 hours after SAH) of hypoxic respiratory failure secondary to a malfunction of the mechanical ventilator. Measurements obtained from this animal before respiratory failure were included in the analysis.

**Cardiac Injury**

As shown in Table 2, RWMA were identified in 8 of 9 SAH dogs and 1 of 5 control dogs (P=0.02). Regional distribution of these RWMA is shown in Table 3. In the 8 SAH dogs, 23 segments developed either hypokinesis (21 segments) or akinesia.2 The midseptum was most frequently involved (56% of SAH dogs), and no involvement of the posterior wall occurred. Mean time of appearance of these RWMA was

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**TABLE 1. Hemodynamic Data**

<table>
<thead>
<tr>
<th>HR, bpm</th>
<th>Pre-SAH</th>
<th>0.5</th>
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<th>2</th>
<th>3</th>
<th>4</th>
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<tr>
<td>SAH</td>
<td>108±17</td>
<td>112±16</td>
<td>112±19</td>
<td>114±19</td>
<td>115±20</td>
<td>117±21</td>
<td>119±12*</td>
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<td>SBP, mm Hg</td>
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<td>97±14</td>
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<tr>
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<td>LAP, mm Hg</td>
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<td>4.1±2.5</td>
<td>5.1±2.1</td>
<td>5.2±1.7</td>
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<td>PAP, mm Hg</td>
<td>16.6±3.7</td>
<td>18.2±2.4</td>
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<td>20.0±2.5</td>
<td>19.7±3.7</td>
<td>19.9±4.1</td>
<td>22.0±3.0*</td>
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<tr>
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<td>19.8±2.9</td>
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<tr>
<td>CO, L/min</td>
<td>2.7±0.8</td>
<td>2.7±0.8</td>
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<td>2.8±1.2</td>
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<tr>
<td>Control</td>
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</table>

SAH indicates subarachnoid hemorrhage; HR, heart rate; SBP, systolic blood pressure; LAP, mean left atrial pressure; PAP, mean pulmonary artery pressure; and CO, cardiac output. Values are mean±SD; n=9 for SAH and n=5 for control.

*P<0.05 for significant changes vs baseline.
1.7 ± 1.4 hours, with a range of 0.5 to 5 hours. RWMA were typically transient, with a mean duration of 1.9 ± 1.1 hours.

On histologic examination, CBN was identified in 6 of 9 SAH dogs and 1 of 5 control dogs (*P = 0.02; Fisher’s Exact Test); †P = NS (SAH vs control dogs; Fisher’s Exact Test); ‡P = 0.001 (correlation between RWMA and CBN in SAH dogs; Fisher’s Z test, r = 0.75).

TABLE 2. Evidence of Cardiac Injury

<table>
<thead>
<tr>
<th>RWMA</th>
<th>CBN</th>
<th>ECG Changes</th>
<th>CPK MB Elevation</th>
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<tr>
<td>SAH dogs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<tr>
<td>2</td>
<td>+</td>
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<td>+</td>
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<td>5</td>
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</tr>
<tr>
<td>9</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Total, %</td>
<td>88.9*</td>
<td>66.7†‡</td>
<td>33.3</td>
</tr>
</tbody>
</table>

| Control dogs |     |             |                 |
| 1    | -   | -           | -               |
| 2    | -   | -           | -               |
| 3    | -   | -           | +               |
| 4    | -   | -           | -               |
| 5    | +   | +           | -               |
| Total, % | 20 20 20 20 0 |

*P = 0.02 (SAH vs control dogs; Fisher’s Exact Test); †P = NS (SAH vs control dogs; Fisher’s Exact Test); ‡P = 0.001 (correlation between RWMA and CBN in SAH dogs; Fisher’s Z test, r = 0.75).

Presence of CBN in the SAH dogs was associated with the development of RWMA (r = 0.75, P = 0.001).

ECG changes that met criteria for new abnormalities occurred in 3 of 9 SAH dogs and 1 of 5 control dogs (Fisher’s Exact Test, P = NS). An example is shown in Figure 2. A significant increase in the CPK-MB fraction did not occur in any of the study animals.

Myocardial Perfusion

No angiographic evidence existed of coronary artery disease or focal epicardial coronary spasm in the SAH and control dogs. MCE was technically adequate in all dogs and abnormal in only 1 SAH dog. In this animal, a single segment with a patchy perfusion pattern was seen at 6 hours after SAH. Although this segment was transiently hypokinetic at 2 to 4 hours after SAH, its systolic function was normal at the time of the abnormal MCE pattern, and MCE showed normal perfusion in contiguous segments with transient RWMA. The MCE perfusion patterns were otherwise normal; an example is shown in Figure 3.

The average global MBF in the study dogs is shown in Figure 4. Average MBF increased in both groups 1 hour after SAH, but no differences existed in the curves for global MBF versus time between the 2 groups. Although mean MBF appeared slightly higher for SAH animals, this did not reach statistical significance (SAH, 1.42 ± 1.17 mL/min · g versus control 0.94 ± 0.29 mL/min · g; P = 0.08).

Average subendocardial/subepicardial MBF ratio for the study dogs is shown in Figure 5, and no differences were seen in the curves for the SAH and control groups. Both groups showed a significant decrease in the ratio during the course of the experiment (P = 0.006 for SAH slope and P = 0.004 for control slope).

To determine whether focal myocardial hypoperfusion was present in segments that developed wall-motion abnormalities, subendocardial MBF in these segments was analyzed separately before and after SAH. No significant difference occurred in mean subendocardial blood flow of these segments after SAH.
Discussion
The cause of cardiac injury that occurs after SAH remains controversial. In clinical studies, myocardial ischemia has been implicated as the cause of ECG changes in LV dysfunction.\textsuperscript{12,15,16} However, substantial evidence from animal models suggests that excessive release of catecholamines from sympathetic nerve terminals in the myocardium is a more likely cause of cardiac injury after SAH.\textsuperscript{2} The exact mechanism of catecholamine-mediated myocardial damage is unknown, although persistent activation of calcium channels, membrane damage, and microvascular spasm have been proposed as causes.\textsuperscript{2} No previous experimental model of SAH has assessed ventricular function and microvascular perfusion simultaneously.

The present study was designed to test the hypothesis that SAH-induced cardiac injury may occur in the absence of myocardial ischemia because of epicardial or microvascular dysfunction. This aim was facilitated by the development of a unique canine model of neurogenic heart disease in which experimental SAH resulted in the development of RWMA of the LV and CBN of the myocardium. These abnormalities occurred in the absence of significant myocardial hypoperfusion at the epicardial or microvascular level.

RWMA of various severities and locations occurred in 89% of SAH dogs. This result was significantly different from control dogs and indicates that RWMA were largely due to the presence of SAH and not methodological issues such as thoracotomy and anesthesia. These results are consistent with those of Elrifai et al.\textsuperscript{17} who found RWMA with variable location and severity in 9 consecutive dogs that underwent experimental SAH. However, that study was uncontrolled and was limited by the use of transesophageal echocardiography, which does not provide standardized views of segmental LV function. In addition, myocardial perfusion was not assessed.

Small changes in heart rate and mean pulmonary artery pressure after SAH were observed over the course of the experiments. However, these hemodynamic changes did not result in a change in cardiac output, and myocardial function or MBF was unlikely to have been significantly affected.

CBN was identified in pathological specimens of 67% of the SAH dogs and only 20% of control dogs. The presence of CBN was significantly correlated with the presence of RWMA in study dogs. Although previous animal and clinical studies of SAH have found evidence of CBN,\textsuperscript{18,19} no prior controlled experimental studies have described the association between CBN and LV systolic dysfunction.

ECG changes occurred in only 33% of SAH dogs. This finding is not surprising, given that previous studies have found poor correlation between ECG changes and LV dys-

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**Figure 2.** Example of ECG changes from an SAH dog. Baseline tracings (left) have isoelectric ST segments. Tracings on the right demonstrate inferior ST depression and lateral ST elevation, which developed 4 hours (4°) after SAH.

**Figure 3.** Example of myocardial contrast echocardiography from a SAH dog. Left, Precontrast image. RV indicates right ventricle. Right, Contrast-enhanced image demonstrates homogeneous perfusion. Arrow indicates a region of transient attenuation that showed normal perfusion in subsequent frames.
function in humans with SAH. Elevation of the CPK-MB fraction did not occur, which suggests that myocardial necrosis was not the cause of the RWMA observed acutely after SAH in the present study. However, CPK-MB might have risen if the time period between SAH and CPK-MB measurement were prolonged.

Coronary angiography demonstrated no evidence of fixed coronary artery stenosis or epicardial coronary spasm to explain the development of observed RWMA. The radiolabeled-microsphere MBF measurements showed no differences in average blood flow between SAH and control dogs. Even when subendocardial MBF data for segments developing RWMA were isolated, no difference between average pre-SAH and post-SAH measurements was noted. Although the subendocardial MBF decreased after SAH in some individual segments, no flows <0.3 mL/min·g were observed, and myocardial infarction is unlikely to occur above this threshold level.21

Normal microvascular perfusion was also demonstrated by MCE in 8 of 9 SAH dogs. In the only reported study of myocardial perfusion after SAH, Szabo et al.11 acquired rest and redistribution planar thallium scans on 19 patients and found reversible defects in 6, but the location and extent of the defects were not described. That study did not include control subjects, and the results may have been confounded by the presence of coronary artery disease, given that angiography was not performed.

One limitation of the present study is the open-chest animal model. This model was developed to facilitate hemodynamic monitoring, the MCE protocol, and measurement of MBF by radiolabeled microspheres. Although it is possible that some of the observed RWMA and CBN may have been due to the effects of anesthesia and surgery, the significantly greater occurrence of RWMA in the SAH versus control dogs is reassuring.

In addition, MCE and MBF measurements were made at only 3 discrete time points after SAH and could be insensitive to changes in blood flow that occur within very small myocardial regions (<0.5 g). Therefore, the possibility that the RWMA were caused by transient myocardial ischemia that occurred between MBF measurement time points or in very small areas cannot be excluded.

The present study was not designed to determine whether catecholamine-mediated damage is the mechanism of cardiac injury after SAH, and the pathogenesis of this syndrome remains unclear. Catecholamines were not measured in the present study because myocardial interstitial levels are difficult to measure without microdialysis techniques22 and serum levels do not always rise after SAH.2

In conclusion, this study used a unique model to demonstrate that LV systolic dysfunction and CBN of the myocardium after experimental SAH can occur in the absence of persistent myocardial hypoperfusion. Clinical studies should be performed to improve current knowledge regarding the pathophysiology and reversibility of LV dysfunction in humans with SAH.

References
Patients with aneurysmal subarachnoid hemorrhage (SAH) frequently have cardiovascular complications that include blood pressure fluctuations, cardiac arrhythmias, and ECG changes. These changes have been attributed to sympathetic hyperactivity that occurs during and after the SAH.1 Arrhythmias and ECG changes may be associated with underlying cardiac damage manifest as contraction-band necrosis and elevated cardiac enzymes. Contraction-band necrosis is a cardiac pathology that may be reversible; that is often found in patients who die after different types of stresses, including SAH; and that is characteristic of heart muscle exposed to excessive catecholamines and intracellular calcium, which leads to a hypercontracted state. Echocardiography showed left ventricular wall motion abnormalities with moderately to severely reduced ejection fractions in 13% of 103 patients from 3 series studied within 6 days of SAH.2–4 These studies specifically excluded patients with preexisting cardiac disease. The patients with abnormal echocardiography usually were poor grade, had episodes of pulmonary edema and hypotension requiring intravenous pressors, and had elevated cardiac enzymes.2–4 It was postulated that sympathetic hyperactivity after SAH leads to a hyperdynamic cardiovascular state with increased left ventricular performance and that elevations in cardiac enzymes indicated inability of the left ventricle to respond to sympathetic stress. The sympathetic hyperactivity also might cause coronary artery spasm and, thereby, produce myocardial ischemia. The problem might be compounded by any preexisting coronary artery or other heart disease.

In the present study, Zaroff et al test the hypothesis that myocardial dysfunction is due to a direct effect of catecholamines on the heart by examination of coronary angiograms and measurement of cardiac blood flow after SAH in dogs.5 They modified the traditional cisternal blood injection by adding thrombin to the blood to promote clotting and “accelerate the development of cardiac injury.” No data are given to support the concept that rapid blood clotting does these things although the phenomena would be worthy of investigation with respect to mechanism if they did occur. Control dogs did not receive injections into the cisterna magna. It would be worthwhile to know whether control animals with saline injection alone had cardiac abnormalities. The first microsphere injection to measure heart blood flow was 30 minutes after the SAH. Blood flow possibly could have been reduced transiently before this time. Intracranial pressure was not measured. Some authorities have suggested that increased intracranial pressure is important to the genesis of cardiopulmonary dysfunction after SAH.4 SAH produced cardiac wall-motion abnormalities and contraction-band necrosis in the absence of changes in coronary arteries or microvascular blood flow, which supports their hypothesis.

The authors of the present study have developed a model that they can now use to determine the mechanism of cardiac injury after SAH and, perhaps, to lead to some method to prevent the injury. Attempts have been made already to do this in humans on the basis of animal studies showing that antidiuretic drugs prevented cardiac injury after SAH.7 A double-blind, randomized, placebo-controlled trial of patients with SAH showed that patients treated with the adrenergic blocker propranolol with or without phentolamine were less likely to die and had better outcome than those who received placebo.8 The patients were operated on late after SAH and blood pressures were not reported. Use of these drugs acutely after SAH is a matter of some concern, because other reports suggest that antihypertensive treatments worsen outcome after SAH.9 Despite this, the concept is an intriguing one and deserves further investigation, because cardiac complications contribute to poor outcome after SAH.10

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References

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