Renal Dysfunction as an Independent Predictor of Outcome After Aneurysmal Subarachnoid Hemorrhage
A Single-Center Cohort Study

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Background and Purpose—Acute kidney injury occurs in 1% to 25% of critically ill patients with small increases in creatinine adversely affecting outcome. We sought to determine the burden of acute kidney injury in patients with aneurysmal subarachnoid hemorrhage and whether this dysfunction affects outcome.

Methods—Between 1996 and 2008, 787 consecutive patients with aneurysmal subarachnoid hemorrhage were enrolled in our prospective database. Demographics, serum creatinine levels, and discharge modified Rankin scores were recorded, and changes in creatinine clearance were calculated. A multiple logistic regression was performed using known predictors for poor outcome after aneurysmal subarachnoid hemorrhage in addition to burden of contrast-enhanced imaging and change in creatinine clearance.

Results—One hundred seventy-nine (23.1%) patients were at risk for renal failure during their hospitalization. In a multivariate model, those patients who developed risk for renal failure were twice as likely to have a poor 3-month outcome (OR, 2.01; \( P = 0.021 \)). Survival curves comparing those not at risk, those at risk (increasing severity classes Risk, Injury, and Failure, and the 2 outcome classes Loss and End-Stage Kidney Disease [RIFLE] R), and those with renal injury or failure (RIFLE I and F) demonstrated that risk of death increases significantly as one progresses through the RIFLE classes (log rank, \( P < 0.0001 \)).

Conclusions—In a large, consecutive series of prospectively enrolled patients with aneurysmal subarachnoid hemorrhage, we demonstrate, using the newly defined RIFLE classification for risk of renal failure, that even seemingly insignificant decreases in creatinine clearance are associated with significantly worse 3-month outcomes. This study highlights the importance of close surveillance of renal function and stresses the value of renal hygiene in the aneurysmal subarachnoid hemorrhage population. (Stroke. 2009;40:00-00.)

Key Words: aneurysm □ outcomes □ renal disease □ SAH

Aneurysmal subarachnoid hemorrhage (aSAH) affects nearly 30,000 individuals each year in the United States. Although early surgical or endovascular protection of ruptured aneurysms and aggressive postoperative management have improved outcomes, it remains a devastating disease with mortality approaching 50% and less than 60% of survivors returning to functional independence.1–3 Cerebral vasospasm and associated delayed neurological deficits accounts for approximately one third of aSAH death and disability, and research has focused heavily on reducing this burden. With improvements in aSAH management, the medical (nonneurological) complications are playing a more prominent role in outcome after aSAH.4–9 The most frequent medical complications include pulmonary edema and pneumonia,4 cardiac arrhythmias,5 electrolyte disturbances,3 and hematologic abnormalities.5,9 These complications can rival the frequency of mortality from neurological complications such as rebleeding and vasospasm.10 Although cardiopulmonary complications after aSAH have been explored at length, little has been done to evaluate the effect of renal dysfunction in this population.

Acute renal failure occurs in 1% to 25% of critically ill patients, and even small increases in serum creatinine (sCr) can adversely affect outcome.11 Renal dysfunction in patients with subarachnoid hemorrhage has been previously reported as occurring in 0.8% to 7% of patients, although a multitude of definitions were used.3 The Acute Dialysis Quality Initiative group has recently devised a multilevel classification of acute renal failure based on changes in sCr or urine output in which the worst of each criterion is used (Figure 1). The
Risk, Injury, and Failure, and the 2 outcome classes Loss and End-Stage Kidney Disease. RIFLE has become the most widely used definition of acute renal failure. Thus, the concept of acute kidney injury (AKI) is not just acute renal failure; it encompasses the entire spectrum from severe to mild conditions, recognizing that small changes in kidney function are associated with significant changes in short- and possibly long-term outcomes.

Patients with aSAH are particularly vulnerable to multi-system organ dysfunction. Even good-grade patients experience lengthy intensive care unit stays, often undergo operative intervention, and are subjected to potentially harmful fluid management to prevent and treat delayed neurological deficits. Furthermore, these patients undergo a significant number of contrast radiographic studies, including CT angiography, CT perfusion, and catheter-based digital subtraction angiography. Radiocontrast material has been closely associated with renal dysfunction and a number of groups have demonstrated significant increases in mortality in patients with radiocontrast-associated AKI. The combination of these factors predisposes these patients to AKI.

This report focuses on the incidence and effect of mild renal dysfunction in one of the largest clinical series of patients with aSAH presented to date in an effort to test the hypothesis that small changes in creatinine clearance (CrCl) are associated with long-term outcome in this patient population.

Materials and Methods

Patient Population

The Columbia University Subarachnoid Hemorrhage Outcomes Project prospectively enrolled 924 consecutive patients with subarachnoid hemorrhage admitted to the Neurological Intensive Care Unit between August 1, 1996, and May 1, 2008. The diagnosis of subarachnoid hemorrhage was established on the basis of admission CT imaging or by xanthochromia of the cerebrospinal fluid. Only patients with documented cerebral aneurysms (787) were included in the study.

Clinical Management

The management of patients with aSAH at our institution has been described in detail previously. Briefly, while the patient was in the neurological intensive care unit, transcranial Doppler 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 intraventricular hemorrhage and a 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. CT angiography and perfusion were used as adjuncts when there was clinical suspicion for vasospasm. All patients were administered 0.9% saline and supplemental 5% albumin to maintain central venous pressure at 8–12 mm Hg, and those with clinical deterioration from delayed cerebral ischemia were treated with hypertensive hypervolemic therapy to maintain systolic blood pressure at 120–200 mm Hg. When significant clinical symptoms persisted despite hypertensive hypervolemic therapy, balloon angioplasty of vasospastic vessels was attempted.

Clinical Assessment

Admission clinical status was evaluated using the Hunt–Hess (H&H) grading scale and Glasgow Coma Score. Complete medical history was recorded on admission. Premorbid functional status was assessed using the modified Rankin Scale (mRS). Admission laboratory values, including sCr were recorded. CrCl was determined with the Cockcroft-Gault equation:

\[
CrCl = \frac{(140-\text{Age}) \times \text{Weight in Kg} \times (0.85 \text{ if female})}{(72 \times sCr)}
\]

Admission and worst CrCl during the index hospitalization were calculated and a percentage change was computed. Delayed ischemic neurological deficits and new infarcts secondary to cerebral vasospasm were recorded by the primary team. Finally, the number of contrast radiographic studies, predominantly contrast-enhanced CT scans of the brain and digital subtraction cerebral angiograms, was recorded. Basic laboratory values were assessed daily, including at a minimum serum chemistries and hematology.

Outcome Measures

Survival and functional outcome was assessed at discharge or 14 days (whichever occurred first), 3 months, and 12 months using the mRS.
Statistical Analysis
Where appropriate, continuous variables were dichotomized based on clinical cut points or median values. The association of mild renal dysfunction (a decrement in CrCl of $\geq 25\%$) was assessed in a univariate analysis using Student $t$-test for analysis of continuous variables and $\chi^2$ for dichotomized variables. Nonparametric tests were used when appropriate. Variables found to be significant on univariate analysis were entered into a multiple logistic regression model based on the clinical relevance of each variable. A model was constructed using a forward-stepwise multiple logistic regression, including all clinically relevant variables with $P<0.25$ in univariate analysis examining the effect of mild renal dysfunction on functional outcome at 3 months after controlling for known predictors of outcome, including, age, H&H grade, clinical vasospasm, pre-existing history of diabetes mellitus or renal failure, and premorbid mRS. Tests for interactions were performed for all clinically significant variables in the multivariate model. Date of death after aSAH was determined as accurately as possible based on medical records and 3- and 12-month follow-up. A Kaplan–Meier curve was created and analyzed by log-rank test. Results are reported as mean $\pm$ SD, and significance was set at $P<0.05$ for all analyses. Data analysis was performed with commercially available statistical software (JMP Version 7; SAS Inc).

Results
Table 1 depicts baseline characteristics of 787 consecutive patients with aSAH that were included in this analysis. The mean age of patients at admission was 55.1 $\pm$ 15 years. Five hundred sixty-two (71.8\%) of the patients were women. Nineteen (2.5\%) of the patients had pre-existing renal disease, and 57 (7.4\%) had diabetes mellitus. Premorbid mRS was less than or equal to one in 726 (94.9\%), and 182 (24.4\%) of the patients presented with poor-grade H&H (Grades IV to V).

Average admission sCr was 0.82 $\pm$ 0.6 mg/dL, and peak sCr was 1.03 $\pm$ 0.9 mg/dL in these patients. Average admission CrCl was 107.7 $\pm$ 49.1 mL/min. Patients received an average of 2.3 $\pm$ 1.6 contrast-enhanced imaging studies. One hundred fifty-nine (20.2\%) patients experienced clinical deterioration secondary to cerebral vasospasm and 96 (12.7\%) developed a new infarct secondary to vasospasm. The majority (73.8\%) were discharged either to home or an acute rehabilitation center. Finally, almost half of the patients (48.7\%) were discharged with a good mRS (0 to 3).

One hundred seventy-nine (23.1\%) patients were at risk for renal failure during their hospitalization as defined by the RIFLE criteria. Table 2 compares demographic, medical characteristics, and outcome between patients at risk and patients not at risk for renal failure. Patients at risk for renal failure were more likely to have a poor-grade admission H&H (31.3\% versus 21.9\%; $P=0.0124$). There were no significant differences, however, in premorbid mRS, age, sex, incidence of clinical vasospasm or new infarct from vasospasm, and history of renal disease or diabetes mellitus. Those who developed risk for renal failure had better baseline renal function as evidenced by admission sCr (0.7 $\pm$ 0.3 versus 0.86 $\pm$ 0.7 mg/dL; $P<0.0001$) and CrCl (121.8 $\pm$ 57.2 versus 105.2 $\pm$ 44.6 mL/min; $P=0.0013$), but went on to develop higher peak sCr (1.35 $\pm$ 1.1 versus 0.93 $\pm$ 0.8 mg/dL; $P<0.0001$). There was no difference in the number of contrast-enhanced imaging studies between these 2 groups. Risk of in-hospital death was 4 times higher in those patients at risk for renal failure (OR, 4.0; $P<0.0001$). Furthermore, those at risk for renal failure were half as likely to be discharged with a good mRS (OR, 0.5; $P<0.0001$) and have a good 3-month mRS (OR, 0.5; $P=0.004$). There was a trend toward worse outcome at 12 months in the at-risk group (OR, 0.6; $P=0.0712$).

Univariate analysis of the primary outcome, poor mRS (4 to 6) at 3 months is shown in Table 3. Patients with poor outcome were older (63 $\pm$ 15 versus 52.4 $\pm$ 13.9 years; $P=0.0001$), less likely to have a premorbid mRS $\leq$ I (87.7\% versus 96.9\%; $P=0.0002$), and more likely to have diabetes mellitus (16.2\% versus 4.1\%; $P<0.0001$). Patients with a poor outcome were 7 times more likely to have a poor-grade admission H&H (48.4\% versus 11.8\%; OR, 7; $P<0.0001$), more than twice as likely to experience a clinical deterioration due to vasospasm (32.4\% versus 17.2\%; OR, 2.32; $P=0.0003$), almost 4 times more likely to develop a new infarct secondary to vasospasm (27.4\% versus 8.8\%; OR, 3.9; $P<0.0001$), and twice as likely to develop risk for renal failure (32.5\% versus 18.1\%; OR, 2.2; $P=0.004$). Admission CrCl was significantly lower in those with poor outcome (96.9 $\pm$ 54 versus 114.4 $\pm$ 46.8 mL/min; $P<0.0001$) and admission (0.98 $\pm$ 1.24 versus 0.77 $\pm$ 0.35; $P=0.0125$) and peak
Creatinine was significantly higher (1.31 ± 0.44 mg/dL; P = 0.0003). Patients with a poor 3-month mRS had a greater number of contrast-enhanced imaging studies (2.8 ± 2.2 versus 2.1 ± 1.4; P = 0.0201). These 2 groups did not differ with regard to sex or history of renal disease.

Significant and clinically relevant factors from the univariate analysis were entered in a multiple logistic regression model to determine independent predictors of poor mRS at 3 months, the results of which are shown in Table 4. The model revealed 7 independent predictors of poor outcome at 3 months. Age and poor admission H&H, known predictors of poor outcome after aSAH, were associated with ORs of 2 per 10-year increase (P < 0.0001) and 10.92 (P = 0.0001), respectively. Per unit increase in the total number of contrast-enhanced imaging studies, the odds of a poor 3-month mRS were increased by 1.27 (P = 0.0003). History of diabetes mellitus was associated with an almost tripling of the odds of poor outcome (OR, 3.6; P = 0.0002). Finally, those patients who developed risk for renal failure were twice as likely to have a poor discharge mRS (OR, 2.01; P = 0.021). Of note, there were no significant interactions between the included variables.

We then performed a second multiple regression using all significant factors from prior analysis and stratified patients into 3 groups based on RIFLE classification (not at risk, at risk, and injury/failure). In this analysis, decline of renal function sufficient to be classified into each advanced group was associated with an increase in the odds of poor outcome (OR, 1.11 and 3.96; P = 0.0038). All previously significant factors remained so in this model.

Kaplan–Meier curves comparing survival in those not at risk, those at risk (RIFLE R), and those with renal injury or failure (RIFLE I and F) are shown in Figure 2. Median survival was greater than the observation period for all groups. However, although the time to 75% survival in those not at risk was still greater than the observation period, it was only 90 days for the at-risk group and 38 days for the injury and failure group. Log-rank test demonstrates a significant (P < 0.0001) difference among the 3 survival curves.

### Discussion

With improvements in neurocritical care, focus has shifted to examining the role of nonneurological complications on outcome after aSAH. In fact, these complications can rival the frequency of morbidity and mortality from neurological complications. Recent studies of patients with brain trauma and aSAH have demonstrated that nearly 80% of these patients develop dysfunction of at least one nonneurological organ system. Not surprisingly, nonneurological organ dysfunction correlates with the severity of neurological impairment. The majority of these studies pay particular attention to cardiopulmonary dysfunction, but the burden of renal, hematologic, and hepatic injuries remains largely unstudied. It is thus paramount that we understand the effect of neurological insults on the remainder of the body and vice versa.

### Table 2. Demographic and Outcome Comparisons for Not-at-Risk and At-Risk Subgroups

<table>
<thead>
<tr>
<th>Variable</th>
<th>Not at Risk for Renal Failure</th>
<th>At Risk for Renal Failure</th>
<th>OR†</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>54.6 ± 14.8*</td>
<td>56.5 ± 15.8*</td>
<td>N/A</td>
<td>NS</td>
</tr>
<tr>
<td>Female</td>
<td>420 (71.0)</td>
<td>137 (76.5)</td>
<td>N/A</td>
<td>NS</td>
</tr>
<tr>
<td>Premorbid Rankin ≤1</td>
<td>562 (95.6)</td>
<td>162 (92.1)</td>
<td>N/A</td>
<td>NS</td>
</tr>
<tr>
<td>Poor-grade admission H&amp;H (Grades IV–V)</td>
<td>130 (21.9)</td>
<td>56 (31.3)</td>
<td>1.35</td>
<td>0.0124</td>
</tr>
<tr>
<td>Pre-existing renal disease</td>
<td>16 (2.7)</td>
<td>3 (1.7)</td>
<td>N/A</td>
<td>NS</td>
</tr>
<tr>
<td>Pre-existing diabetes mellitus</td>
<td>39 (6.7)</td>
<td>17 (9.8)</td>
<td>N/A</td>
<td>NS</td>
</tr>
<tr>
<td>Admission sCr, mg/dL</td>
<td>0.86 ± 0.70</td>
<td>0.70 ± 0.30</td>
<td>N/A</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Admission CrCl, mL/min</td>
<td>105.2 ± 44.6*</td>
<td>121.8 ± 57.2*</td>
<td>N/A</td>
<td>0.0013</td>
</tr>
<tr>
<td>Total no. of contrast-enhanced imaging studies</td>
<td>2.3 (1.6)</td>
<td>2.4 (1.7)</td>
<td>N/A</td>
<td>NS</td>
</tr>
<tr>
<td>In-hospital death</td>
<td>50 (8.4)</td>
<td>48 (26.8)</td>
<td>4.0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Clinical vasospasm</td>
<td>111 (18.7)</td>
<td>44 (24.6)</td>
<td>N/A</td>
<td>NS</td>
</tr>
<tr>
<td>New infarct secondary to vasospasm</td>
<td>65 (11.5)</td>
<td>28 (16)</td>
<td>N/A</td>
<td>NS</td>
</tr>
<tr>
<td>14-day outcome</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mRS = 3 (good outcome)</td>
<td>316 (53.3)</td>
<td>61 (34.3)</td>
<td>0.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>3-month outcome</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mRS = 3 (good outcome)</td>
<td>362 (80.6)</td>
<td>80 (67.8)</td>
<td>0.5</td>
<td>0.004</td>
</tr>
<tr>
<td>12-month outcome</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mRS = 3 (good outcome)</td>
<td>359 (90.0)</td>
<td>79 (63.2)</td>
<td>0.6</td>
<td>0.0712</td>
</tr>
</tbody>
</table>

*Mean ± SD.
†OR of at-risk versus not-at-risk subgroups.
N/A indicates not applicable; NS, nonsignificant.

Results are shown as no. of patients with percentage of cohort in parentheses, except as noted.

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In a series of 787 consecutively treated patients with aSAH, we demonstrate that a seemingly inconsequential decrement in renal function can adversely affect outcome independent of other known predictors. To our knowledge, this is the first study focusing on the effects of renal dysfunction as defined by the RIFLE criteria in the aSAH population. The need for a system to standardize and classify renal dysfunction was fulfilled by the recently developed RIFLE criteria. In addition, the need to classify the severity of renal dysfunction was fulfilled by the recently developed classification.13 In light of this new classification, the syndrome rather than only considering its most severe class of R, 5% to 27% I, and 3.5% to 28% F.13,21,22 These increasing RIFLE classes were associated with a nearly linear increment in a number of unique clinical settings.23 Studies by Gottlieb et al24 and Smith et al25 demonstrated an increase in RIFLE classes were associated with a nearly linear increment in mortality and length of stay with small increases in sCr in patients admitted with congestive heart failure. Lassnigg et al26 and Loef et al27 explored this phenomenon in cardiac and noncardiac surgery patients, respectively, and concluded that elevations as small as 25% in sCr increase the risk of short- and long-term mortality. Recently, Chertow and colleagues extended these findings to a large cohort of hospitalized patients and showed that an increase in sCr of 0.3 to 0.4 mg/dL is associated with a 70% increase in the risk of death.23

We used the RIFLE criteria to determine which patients were at risk for renal failure based on a decrement in estimated CrCl of >25%. Consistent with previous reports in the literature, 23.1% of patients developed risk for renal failure during their hospitalization.13,21,22 As might be expected, these individuals were older and more frequently noncardiac surgery patients, respectively, and concluded that elevations as small as 25% in sCr increase the risk of short- and long-term mortality. Recently, Chertow and colleagues extended these findings to a large cohort of hospitalized patients and showed that an increase in sCr of 0.3 to 0.4 mg/dL is associated with a 70% increase in the risk of death.23

There was significantly worse discharge and 3-month outcome and a trend toward worse 12-month outcome in those at risk for renal failure in our aSAH cohort. In fact, those at risk were nearly half as likely to have a good outcome at 12 months than those not at risk. In a more parsimonious multiple logistic regression model controlling for known predictors of outcome, being at risk for renal failure was associated with a doubling of the likelihood of poor outcome at 3 months. Importantly, across all H&H grades, a decrement in CrCl ≥25% is associated with a significantly worse 3-month outcome. Survival analysis revealed that patients at risk for renal failure were 60% as likely to be alive at 1 year than patients not at risk. As demonstrated by other groups,

### Table 3. Univariate Analysis of Outcome at 3-Month Follow-Up

<table>
<thead>
<tr>
<th>Variable</th>
<th>Good 3-Month Rankin</th>
<th>Poor 3-Month Rankin</th>
<th>OR†</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>52.4±13.9*</td>
<td>63±15*</td>
<td>N/A</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Female</td>
<td>320 (72.1)</td>
<td>95 (75.4)</td>
<td>N/A</td>
<td>NS</td>
</tr>
<tr>
<td>Premorbid Rankin ≤1</td>
<td>434 (96.9)</td>
<td>107 (87.7)</td>
<td>0.23</td>
<td>0.0002</td>
</tr>
<tr>
<td>Poor-grade admission H&amp;H</td>
<td>53 (11.8)</td>
<td>61 (48.4)</td>
<td>7</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Pre-existing renal disease</td>
<td>10 (2.3)</td>
<td>7 (6)</td>
<td>N/A</td>
<td>NS</td>
</tr>
<tr>
<td>Pre-existing diabetes</td>
<td>18 (4.1)</td>
<td>19 (16.2)</td>
<td>4.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Admission Cr, mg/dL</td>
<td>0.77±0.35*</td>
<td>0.98±1.24*</td>
<td>N/A</td>
<td>0.0125</td>
</tr>
<tr>
<td>Admission CrCl, mL/min</td>
<td>114.4±46.8*</td>
<td>96.9±54*</td>
<td>N/A</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Peak creatinine</td>
<td>0.89±0.44*</td>
<td>1.31±1.6*</td>
<td>N/A</td>
<td>0.0030</td>
</tr>
<tr>
<td>CrCl decrease ≥25%</td>
<td>80 (18.1)</td>
<td>38 (32.5)</td>
<td>2.2</td>
<td>0.0040</td>
</tr>
<tr>
<td>Clinical vasospasm</td>
<td>77 (17.2)</td>
<td>41 (32.4)</td>
<td>2.32</td>
<td>0.0003</td>
</tr>
<tr>
<td>New infarct secondary to vasospasm</td>
<td>38 (8.8)</td>
<td>34 (27.4)</td>
<td>3.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Total contrast-enhanced imaging studies</td>
<td>2.2±1.4*</td>
<td>2.8±2.2*</td>
<td>N/A</td>
<td>0.0201</td>
</tr>
</tbody>
</table>

Results are shown as no. of patients with percentage of cohort in parentheses, except as noted.

*Mean±SD.
†Per unit increase.
N/A indicates ; NS, nonsignificant.

### Table 4. Independent Predictors of Poor 3-Month Outcome

<table>
<thead>
<tr>
<th>Covariates</th>
<th>OR</th>
<th>95% CIs</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>2*</td>
<td>1.05–1.09</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Total scans</td>
<td>1.27†</td>
<td>1.1–1.48</td>
<td>0.0013</td>
</tr>
<tr>
<td>Poor admission H&amp;H</td>
<td>6.92</td>
<td>N/A</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Premorbid mRS ≤1</td>
<td>0.28</td>
<td>N/A</td>
<td>0.0184</td>
</tr>
<tr>
<td>Risk of renal failure</td>
<td>2.01</td>
<td>N/A</td>
<td>0.021</td>
</tr>
<tr>
<td>New infarct secondary to vasospasm</td>
<td>3.6</td>
<td>N/A</td>
<td>0.0002</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2.78</td>
<td>N/A</td>
<td>0.0216</td>
</tr>
</tbody>
</table>

*Per 10-year increase.
†Per unit increase.
N/A indicates.
our analyses revealed a significant relationship between worse outcome and increasing RIFLE classification. RIFLE \textsuperscript{R} was associated with a doubling of the odds of poor outcome, and becoming RIFLE \textsuperscript{I} or \textsuperscript{F} was associated with an almost quadrupling of the risk of poor outcome.

Although the results are convincing, we recognize that there are several limitations of our study. Retrospective analysis of prospectively collected data has many of the methodological shortcomings of purely retrospective studies and, as such, it remains difficult to accurately assess causality. We attempted to control for disease severity, but given the retrospective nature of the analyses, we are unable to account for all possible confounders. It is possible that the decrease in CrCl is simply indicative of disease severity, and these patients are more likely to receive nephrotoxic drugs, contrast-enhanced imaging studies, experience hypotension and hypoxia, and have concomitant injury in other organ systems. Published studies, however, have demonstrated a consistently high relative risk associated with AKI despite adjustment for comorbid conditions.\textsuperscript{23} In addition, our analyses demonstrate that AKI increased the odds of a poor outcome at all H&E levels. Although residual confounding could lessen the magnitude of the risk estimates, additional covariates would be unlikely to extinguish the increased odds of poor outcome. Furthermore, we lacked sufficient data to identify the etiology or type of renal failure and were unable to quantify urine output.

Regardless, we feel that our study findings are of significant clinical interest. A decrease of 25% in creatinine clearance can represent an increase in CrCl of as little as 0.2 mg/dL, a change that rarely prompts alteration of the treatment course. As we continue to improve the neurological management of patients with aSAH, there is a shift toward increasing disease severity and consequently more critically ill patients. These poor-grade patients with aSAH are invariably managed in an intensive care unit setting, undergo surgical or endovascular procedures, have diminished mental capacity, and are frequently intubated. These factors combine to place these patients at particular risk for renal complications. This study highlights the importance of early recognition of renal risk and prompts clinicians to practice renal hygiene. That is, avoidance of redundant contrast-enhanced imaging studies, adequate hydration and renal protection strategies, and frequent screening of medication lists for potentially nephrotoxic drugs and dose adjustment for those with renal impairment.

**Conclusion**

In a large, consecutive series of prospectively enrolled patients with aSAH, we demonstrate, using the newly defined RIFLE classification for risk of renal failure, that even seemingly insignificant decreases in creatinine clearance are associated with significantly worse 3-month outcomes. Whether renal dysfunction is merely a marker of disease severity or an independent predictor of poor outcome cannot be elucidated from retrospective analysis. Nevertheless, this study highlights the importance of close surveillance of renal function and stresses the value of renal hygiene in the aSAH population.

**Disclosures**

None.

**References**


Renal Dysfunction as an Independent Predictor of Outcome After Aneurysmal Subarachnoid Hemorrhage. A Single-Center Cohort Study

Stroke. published online May 21, 2009;
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

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http://stroke.ahajournals.org/content/early/2009/05/21/STROKEAHA.108.545210.citation

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