Incidence and Outcomes in Acute Kidney Injury: A Comprehensive Population-Based Study

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Epidemiologic studies of acute kidney injury (AKI) and acute-on-chronic renal failure (ACRF) are surprisingly sparse and confounded by differences in definition. Reported incidences vary, with few studies being population-based. Given this and our aging population, the incidence of AKI may be much higher than currently thought. We tested the hypothesis that the incidence is higher by including all patients with AKI (in a geographical population base of 523,390) regardless of whether they required renal replacement therapy irrespective of the hospital setting in which they were treated. We also tested the hypothesis that the Risk, Injury, Failure, Loss, and End-Stage Kidney (RIFLE) classification predicts outcomes. We identified all patients with serum creatinine concentrations ≥150 μmol/L (male) or ≥130 μmol/L (female) over a 6-mo period in 2003. Clinical outcomes were obtained from each patient’s case records. The incidences of AKI and ACRF were 1811 and 336 per million population, respectively. Median age was 76 yr for AKI and 80.5 yr for ACRF. Sepsis was a precipitating factor in 47% of patients. The RIFLE classification was useful for predicting full recovery of renal function (P < 0.001), renal replacement therapy requirement (P < 0.001), length of hospital stay [excluding those who died during admission (P < 0.001), and in-hospital mortality (P = 0.035). RIFLE did not predict mortality at 90 d or 6 mo. Thus the incidence of AKI is much higher than previously thought, with implications for service planning and providing information to colleagues about methods to prevent deterioration of renal function. The RIFLE classification is useful for identifying patients at greatest risk of adverse short-term outcomes.


The International Acute Dialysis Quality Initiative (ADQI) (12) group suggested RIFLE (risk, injury, failure, loss, ESRD) classification for AKI and ACRF (Table 1) and suggested that this should be tested in large data sets. No population-based studies have been carried out to test the ability of this classification to predict outcomes.

We aimed to determine the incidence and factors that affect the development and outcomes of AKI and ACRF in a defined population that included patients who had or had not required RRT and irrespective of the hospital setting in which they were treated. We aimed to test the hypotheses that the incidence of AKI and ACRF is much higher than previously estimated and that the RIFLE classification predicts short- and long-term outcomes.

Materials and Methods

We carried out a retrospective cohort study in the Grampian region of Scotland (population 523,390). There are 3 hospitals in this area and 2 biochemistry laboratories, which are electronically linked.

For the purpose of this study, we defined a “threshold” serum
creatinine value of 150 μmol/L in men or 130 μmol/L in women. We identified all adult patients (>15 yr old) with serum creatinine value more than or equal to the threshold during a 6-mo period (January 1, 2003, through June 30, 2003). This serum creatinine value was termed the “index creatinine.” Using the abbreviated Modification of Diet in Renal Disease (MDRD) equation (13,14), we estimated the GFR and applied the RIFLE classification (Table 1). We used the rise in serum creatinine concentration or fall in GFR (whichever was greater) to assign a category in the RIFLE classification; we did not use urine output as a criterion for classification, because it was not possible to obtain accurate records of urine output. We studied the R, I, and F categories; the last 2 categories (L and E) are clinical outcomes.

**AKI Group**

When serum creatinine had been measured in the 6 mo before the date of index creatinine, this was taken as baseline creatinine. Patients were classified as having AKI when baseline serum creatinine was below the threshold and subsequently rose by a factor of 1.5 or more or the GFR was reduced by 25% or more. We also noted the highest serum creatinine that the patient had had during the episode of AKI (“maximum creatinine”). When a baseline serum creatinine was not available but creatinine subsequently fell from the maximum creatinine by a factor of 1.5 or more or to a value below threshold, these patients were also defined as having AKI.

Patients were excluded when baseline was not available and the patient died before renal recovery. They also were excluded when creatinine rise was less than a factor of 1.5 or rise was not sustained for 24 h.

**ACRF Group**

The ADQI group recommends separate criteria for the diagnosis of ACRF. They assigned these patients to the Fc category (where F is failure and C is CKD) when their serum creatinine had increased to 350 μmol/L/L. The ADQI group did not assign a category to those in whom serum creatinine did not rise as high as 350 μmol/L/L.

Patients in our study were defined as having chronic kidney disease (CKD) when they had three creatinine values that were above threshold before the index creatinine and each value was separated by at least 1 mo. Biochemistry database was searched from 1996 onward to obtain serum creatinine values to define CKD.

We used the following classification of ACRF in this study:

1. Risk (R-ACRF): serum creatinine had risen by a factor of 1.5 or more from the baseline or GFR reduced by 25% or more but serum creatinine had not reached 350 μmol/L.

2. Injury (I-ACRF): serum creatinine had risen by a factor of 2 or more, or GFR reduction was 50% or more but serum creatinine had not reached 350 μmol/L.

3. Failure to recover: Dialysis dependent at 90 d.

4. Injury in ESRD (I-ESRD): serum creatinine had risen by a factor of 2 or more, or GFR reduction was 50% or more but serum creatinine had not reached 350 μmol/L.

5. Failure to recover: Dialysis dependent at 90 d.

6. Loss (L): Persistent AKI.

Table 1. RIFLE classification

<table>
<thead>
<tr>
<th>Category</th>
<th>GFR Criteria</th>
<th>UO Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk (R)</td>
<td>Increased creatinine ×1.5 or GFR ↓ by 25%</td>
<td>UO &lt;0.5 ml/kg per h × 6 h</td>
</tr>
<tr>
<td>Injury (I)</td>
<td>Increased creatinine ×2 or GFR ↓ by 50%</td>
<td>UO &lt;0.5 ml/kg per h × 12 h</td>
</tr>
<tr>
<td>Failure (F)</td>
<td>Increased creatinine ×3 or GFR ↓ by 75% or creatinine ≥350 μmol/L (rise at least 44 μmol/L)</td>
<td>UO &lt;0.3 ml/kg per h × 24 h or anuria × 12 h</td>
</tr>
<tr>
<td>Loss (L)</td>
<td>Persistent AKI &gt;4 wk</td>
<td>ES</td>
</tr>
<tr>
<td>ESRD (E)</td>
<td>ESRD &gt;3 mo</td>
<td></td>
</tr>
</tbody>
</table>

*AKI, acute kidney injury; RIFLE, risk, injury, failure, loss, ESRD; UO, urine output.

**Data Collection**

Data including demographic details, background comorbid conditions, precipitating factors, duration of hospital stay, requirement for and mode of RRT, and date of death were extracted from patient records. Patients were classified into low-, medium-, and high-risk categories using the Khan index (15) (low risk: Age <70 and no comorbid illness; medium risk: Age >70 and <80, or age <80 with one comorbid illness, or age <70 with diabetes; high risk: Age >80, or any age with two or more comorbidities, or any age with malignancy).

**Statistical Analyses**

Data were analyzed using SPSS (Release 14.0.0; SPSS, Chicago, IL). For categorical variables, groups were compared using the χ² test or Fisher exact test when expected values of <5 were obtained. For age and duration of hospital stay, group medians were compared using Mann-Whitney U tests (between AKI and ACRF) or Kruskal-Wallis tests (among R, I, and F categories and among Khan’s index low, medium, and high categories).

**Results**

**Demographics and Comparison of AKI and ACRF Groups**

A total of 5321 patients were identified as having a creatinine that was more than or equal to the threshold value. A total of 474 patients were classified as having AKI, and 88 were classified as having ACRF. This equates to an annual incidence of 1811 and 336 pmp, respectively. The breakdown of the groups is shown in Figure 1.

A total of 393 (83%) of those with AKI had a baseline creatinine value available on the biochemistry database. A total of 81
(17%) patients did not have a baseline creatinine available, but, after recovering from AKI, their creatinine both fell by a factor of at least 1.5 and fell below our threshold value.

Patients in the ACRF group were older than those with AKI \((P = 0.003)\). Renal imaging was performed more often in the ACRF group \((P < 0.001)\), and a greater proportion of patients were treated by nephrologists in this group \((P < 0.001)\). Median duration of stay in hospital was longer in the AKI than in the ACRF group \((P = 0.009)\). A significantly greater proportion of patients had full recovery of renal function in the AKI group \((P < 0.001)\). There were no significant differences in gender, RRT requirement, and mortality (in-hospital and 90 d) between the two groups. Most patients in both groups were in the high-risk category using Khan’s index. Only 45 (9.5%) patients with AKI and 3 (3.4%) patients with ACRF were treated in the ICU (Table 2).

Precipitating Factors and Comorbid Conditions
Sepsis was the most frequent precipitating factor (47%) followed by hypovolemia (32%). A total of 39% had more than one precipitating factor for the development of AKI and ACRF. Comorbidities are shown in Table 3.

Outcomes
Mortality. Mortality rose to 50% by 6 mo in those with AKI and to 63% in those with ACRF (Table 2). Significantly more...
patients died during hospital admission in the F category of the AKI group (P = 0.035) (Table 4; Figure 2). Mortality (except at 6 mo) was not significantly different across RIFLE-ACRF categories (Table 4).

In those with AKI, 26% of the low-risk group died, and mortality increased to 42% in the medium-risk and 56% in the high-risk groups at 6 mo. Overall, there was a highly significant association between Khan’s index and mortality at 6 mo (P < 0.001; Table 5). A similar trend was observed among patients with ACRF, with mortalities of 0 (there were only four patients in the low-risk group), 56, and 68%, respectively, for those in the ACRF group (P = 0.016).

**Renal Recovery.** Full renal recovery was achieved in 321 (68%) of those in the AKI group; 24 (5%) partially recovered, and in 127 (27%), recovery could not be determined because the patient died in the acute phase. Recovery in the F category was significantly lower (P < 0.001). Only two patients remained on dialysis for >90 d. After exclusion of the 127 patients in whom it was not possible to determine the recovery because they died in the acute phase of their illness, 92.5% had full renal recovery, 7% had partial recovery, and 0.6% had no recovery.

In contrast, in the ACRF group, full recovery was achieved in only 31 (35%), partial recovery was achieved in 14 (16%), and 40 (45%) patients died in the acute phase. No significant differences were observed in the proportions with full recovery across the RIFLE-ACRF categories (Table 4); three patients had no recovery of their renal function. After exclusion of the 40 patients in whom it was not possible to determine recovery, 65% had full recovery, 29% had partially recovery, and 6% had no recovery.

**Patients Who Received RRT.** Thirty-seven (8%) patients with AKI received RRT; 23 (62%) of these had their first dialysis in the ICU, 13 (35%) in the renal unit, and one in a surgical high-dependency unit. Nineteen (51%) had hemodialysis and 18 (49%) had hemofiltration as the first mode of RRT. Twenty-one (57%) of those who received RRT died. Only two patients were on RRT at 90 d. Most patients who received RRT were in the F category (P < 0.001).

Eleven (13%) of those in the ACRF group received RRT. Nine (82%) patients received dialysis in the renal unit, one in the ICU, and one in a coronary care unit. Ten received hemodialysis and one received hemofiltration; five (45%) of those who received RRT had died by 6 mo. Most patients who received RRT were in the Fc category.

**Referral to Nephrologists.** Only 25% of those in the AKI group were referred to a nephrologist. A significantly greater proportion of patients were referred from the F category (P < 0.001). In contrast, 51% of the ACRF group were referred, and there were no significant differences in the rates of referral between RIFLE-ACRF categories (Table 4).

**Duration of Hospital Stay.** The median duration of stay for AKI was 17 d; this was significantly shorter in the R category (P = 0.047). However, among those who survived to leave the hospital, the duration of stay increased across RIFLE categories, being longest in F (P = 0.001). Median duration of stay was difficult to interpret in the ACRF group because of the small number in the R and I categories, especially after exclu-

### Table 4. AKI and ACRF outcomes: Effect of RIFLE

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>AKI Group</th>
<th>ACRF Group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All</td>
<td>F</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>P</td>
</tr>
<tr>
<td>Hospital stay (d; median)</td>
<td>17 (9 to 33)</td>
<td>15.5 (8.3 to 26.0)</td>
</tr>
<tr>
<td>90 d mortality (%)</td>
<td>105 (11)</td>
<td>26 (48)</td>
</tr>
<tr>
<td>Full renal recovery (%)</td>
<td>964 (68)</td>
<td>1 (6)</td>
</tr>
<tr>
<td>In-hospital mortality (%)</td>
<td>874 (66)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>6-mo mortality (%)</td>
<td>909 (63)</td>
<td>2 (1)</td>
</tr>
</tbody>
</table>

**Excluding those who died during admission.
In a prospective study in England, which, unlike those quoted earlier, took place. The combined annual incidence of AKI and ACRF was 2147 pmp, very much higher than all previous published estimates. The RIFLE classification predicted the probability of making a full renal recovery, the need for RRT, the length of hospital stay, and in-hospital mortality. It did not, however, predict the long-term outcomes of mortality at 90 d and 6 mo.

In a Spanish study (10), the incidence of AKI was calculated at 209 pmp/yr; patients who were treated in tertiary care hospitals with a serum creatinine >177 μmol/L were included. Retrospective studies in the UK reported an incidence in those with a serum creatinine ≥300 μmol/L of 620 pmp/yr (6) and 140 pmp/yr in those with serum creatinine ≥500 μmol/L (9). In a prospective study in England, which, unlike those quoted previously included patients with ACRF, the incidence was 545 pmp/yr in those with serum creatinine of >300 μmol/L (5). The incidence in this study is higher, probably reflecting the lower serum creatinine value for entry and that all patients in a defined geographic area were included. The incidence rate in the Spanish study is lower than in all of the UK studies despite its lower serum creatinine value at entry, possibly because many patients may have been treated in hospitals other than the tertiary care hospitals or because there may be a lower incidence of acute renal failure in Spain. A recent large study from the United States gave an incidence of 288 pmp, although this was based on International Classification of Diseases, Ninth Revision coding at discharge rather than on creatinine values (11). The age distribution of the United Kingdom is similar to that in Spain, with approximately 16% of the population older than 65 yr; it is slightly lower in the United States (12.4%) (16), although not sufficient to explain the difference in incidence. The reported incidence of AKI in the literature therefore varies considerably and depends on how AKI is defined, whether ACRF is included, and whether all patients in the population studied are included. In our population-based study, the incidence is much higher, with important implications for service planning.

The mean age in the study by Liano and Pascual (10) was 64, in the study by Stevens et al. was 73 (5) and in an American ICU-based study was 67 (17). Waikar et al. (11) reported median age in patients who were identified between 1998 and 2002 as 72; patients in our study had a median age of 77, and this was higher in those with ACRF. In a previous study, the median age in those who required RRT was reported to be 65.8 yr in AKI and 74.9 in ACRF (8). The high median age in our study reflects inclusion of all patients with AKI or ACRF regardless whether they needed RRT or whether they were cared for in the ICU. AKI and ACRF are emerging as diseases of the elderly; therefore, their incidence is likely to continue to rise.

Sepsis was the most frequent precipitating factor (47%) for AKI in our study, similar to the findings of others (8,11,18). We also found that >80% of patients had at least one comorbid illness and that the majority, approximately 70% of patients with AKI, were in the high-risk group. This is slightly higher than the 65% (of 310 patients) in the high-risk group in a study in the same geographic area in 1989 to 1990, although, in that study, the entry criterion for the high-risk group was defined geographic area in 1989 to 1990, although, in that study, the entry criterion for the high-risk group was lower serum creatinine value for entry and that all patients in a defined geographic area were included. The incidence rate in the Spanish study is lower than in all of the UK studies despite its lower serum creatinine value at entry, possibly because many patients may have been treated in hospitals other than the tertiary care hospitals or because there may be a lower incidence of acute renal failure in Spain. A recent large study from the United States gave an incidence of 288 pmp, although this was based on International Classification of Diseases, Ninth Revision coding at discharge rather than on creatinine values (11). The age distribution of the United Kingdom is similar to that in Spain, with approximately 16% of the population older than 65 yr; it is slightly lower in the United States (12.4%) (16), although not sufficient to explain the difference in incidence. The reported incidence of AKI in the literature therefore varies considerably and depends on how AKI is defined, whether ACRF is included, and whether all patients in the population studied are included. In our population-based study, the incidence is much higher, with important implications for service planning.

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Figure 2. Percentage of mortality among patients with AKI by RIFLE (risk, injury, failure, loss, ESRD) categories.
was a serum creatinine \( \geq 300 \, \text{\mu mol/L} \) (6). Another study of patients with AKI with no other organ failure and a serum creatinine \( \geq 500 \, \text{\mu mol/L} \) that was known to renal or ICU staff found that 46% were in the high-risk group (19). The differences among studies may in part reflect the serum creatinine value at entry, whether patients had single or multiple organ failure, or whether only those who were referred to a nephrologist were included. The proportion of patients who have AKI/ACRF and are elderly and/or have significant comorbidity, however, is high. The absolute numbers of such patients are increasing along with the technical ability to treat them. In addition to standardizing the definition of AKI and data collection methods, we must determine the need for and appropriate use of critical care resources for this group of patients.

A recent survey in Europe showed that the RIFLE classification is being used more commonly (20). Two studies (21,22) showed a higher number of patients in the F category than ours, but both of these were in an ICU setting, where more advanced AKI would be expected. This study differs from all others by including patients who were identified from a single biochemistry laboratory database that serves the whole population and setting a relatively low threshold creatinine value for entry. However, if patients' creatinine values had never risen above this threshold during the 6-mo identification period (i.e., those with very mild AKI), then they would have been excluded from our study. This may explain why the number of patients in the R category was lower than that in the I category. An ICU-based study in the United Kingdom showed similar percentages in R and I categories (22), and another study found that \(<10\%\) were in the R category, but that study was restricted to those who required RRT in the ICU (21). Therefore the percentages in each category will vary with the question being posed by the investigator and the patient group being studied.

A systematic review reported overall mortality of 50% in various groups of patients who had AKI and were measured at various time points (23). The mortality figures in our study are consistent with those of Stevens et al. (5). In our study, the RIFLE classification was able to predict in-hospital mortality but not mortality at 90 d or 6 mo. In contrast, comorbidity conditions predicted mortality at 90 d and 6 mo but not mortality that occurred in hospital, showing that the severity of renal impairment predicts early and comorbidity predicts later mortality.

RRT requirement was significantly higher in those in the F group than in the R and I groups (\( P < 0.001 \)); this was also found in the ICU-based studies in the United Kingdom (22) and Sweden (21). Although the referral rate was higher in F, this did not completely explain the higher rates of RRT that were observed in the F category—considering only those who were referred, there was a much higher likelihood of receiving RRT when they were in the F category than in the R or I categories (Table 4).

When the patients who died in hospital were excluded, full recovery of renal function was very high in those with AKI (92.5%). This is likely to reflect that almost all of the precipitating factors for AKI in this group of patients would have led to acute tubular necrosis, which then recovered irrespective of its severity, making it inappropriate to apply the RIFLE classification to this outcome. In contrast, creatinine values were reduced to previous levels in only 65% of those who had background CKD and survived their acute illness. Few studies have reported renal recovery in patients with AKI, but some, such as ours, have shown that the majority will recover sufficient renal function (24).

Median duration of stay in this study was shorter than in two ICU-based studies (16,25) in which the patients were likely to have been more severely ill. It was closer to that in a study of patients who required RRT and were treated in all hospital environments (8). In our study, the RIFLE classification was able to predict length of stay, making it useful for service planning.

For the binary outcomes, logistic regression was used to adjust for the possible confounding factors: age, gender, and comorbidities. RIFLE was still found to be significantly associated with in-hospital mortality, full renal recovery, need for RRT, and referral.

In this study, the numbers with ACRF were small and association between categories and outcomes (except 6-mo mortality) could not be demonstrated. There were only 58 patients in the Fc group, although this number was increased by 30 using our wider definition of ACRF. We still may have missed a significant number of patients because those with background CKD would require a considerable increase in creatinine to enter this classification (e.g., a baseline creatinine of 200 \( \mu \text{mol/L} \) requires a rise to 300 \( \mu \text{mol/L} \) for entry into the R category). Appropriate criteria for ACRF therefore requires more discussion and possibly further studies.

**Conclusion**

This population-based study showed that incidence of AKI is much higher than previously thought, with important implications for service planning and the provision of information to colleagues so that early action can be taken to prevent deterioration of renal function. We also defined a population group in which early interventions can be tested. The RIFLE classification was useful for predicting in-hospital mortality, the need for RRT, the length of hospital stay, and the likelihood of recovery of renal function but not survival at 90 d or 6 mo. This classification therefore should be used to identify the patients who are at greatest risk for adverse short-term outcomes.

**Acknowledgments**

We thank Kidney Research UK for funding this project. Part of this research was presented at the Renal Association (May 3 to 5, 2006; UK) and at the European Renal Association meeting (July 15 to 18; 2006). We are grateful to Alan Broad for setting up the database and Carol Ritchie for all her hard work throughout the process.

**Disclosures**

None.

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Access to UpToDate on-line is available for additional clinical information at http://www.jasn.org/