

An Assessment of the Acute Kidney Injury Network Creatinine-Based Criteria in Patients Submitted to Mechanical Ventilation

Raúl Lombardi,* Nicolás Nin,^{††} José A. Lorente,^{††} Fernando Frutos-Vivar,^{††} Niall D. Ferguson,[§] Javier Hurtado,^{||} Carlos Apezteguia,[¶] Pablo Desmery,^{**} Konstantinos Raymondos,^{††} Vinko Tomcic,^{##} Nahit Çakar,^{§§} Marco González,^{|||} José Elizalde,^{¶¶} Peter Nightingale,^{***} Fekri Abroug,^{†††} Manuel Jibaja,^{†††} Yaseen Arabi,^{§§§} Rui Moreno,^{|||} Dimitros Matamis,^{¶¶¶} Antonio Anzueto,^{¶¶¶¶} and Andrés Esteban,^{††} for the VENTILA Group

Summary

Background and objectives The aim of our study was to assess the new diagnostic criteria of acute kidney injury (AKI) proposed by the Acute Kidney Injury Network (AKIN) in a large cohort of mechanically ventilated patients.

Design, setting, participants, & measurements This is a prospective observational cohort study enrolling 2783 adult intensive care unit patients under mechanical ventilation (MV) with data on serum creatinine concentration (SCr) in the first 48 hours. The absolute and the relative AKIN diagnostic criteria (changes in SCr ≥ 0.3 mg/dl or $\geq 50\%$ over the first 48 hours of MV, respectively) were analyzed separately. In addition, patients were classified into three groups according to their change in SCr (Δ SCr) over the first day on MV (Δ SCr): group 1, Δ SCr ≤ -0.3 mg/dl; group 2, Δ SCr between -0.3 and $+0.29$ mg/dl; and group 3, Δ SCr $\geq +0.3$ mg/dl). The primary end point was in-hospital mortality, and secondary end points were intensive care unit and hospital length of stay, and duration of MV.

Results Of 2783 patients, 803 (28.8%) had AKI according to both criteria: 431 only absolute (AKI_A), 362 both relative and absolute (AKI_{R+A}), and 10 only relative. The relative criterion identified more patients when baseline SCr (SCr₀) was <0.9 mg/dl and the absolute when SCr₀ was >1.5 mg/dl. The diagnosis of AKI was associated with mortality.

Conclusions Our study confirms the validity of the AKIN criteria in a population of mechanically ventilated patients and the criteria's relationship with the baseline SCr.

Clin J Am Soc Nephrol 6: 1547–1555, 2011. doi: 10.2215/CJN.09531010

Introduction

Acute kidney injury (AKI) is a frequent and serious clinical condition in critically ill patients that is associated with an increased need for renal replacement therapy (RRT), a longer hospital stay, a higher cost, a higher incidence of end-stage renal disease, and a higher early and late mortality (1–3). Thus, early recognition of AKI is important to optimize therapy to prevent or to minimize the associated adverse outcomes. Yet, unfortunately, there is still no agreement regarding an operative definition of AKI. More than 30 definitions can be found in the literature, which makes it difficult to compare studies on epidemiology, prevention, or treatment of AKI (4). Efforts to develop a consensus definition have been made by the Acute Dialysis Quality Initiative (ADQI) (5). This group proposed a definition and classification of AKI based on changes in serum creatinine concentration (SCr) and/or urine output, which is known as the Risk, Injury, Failure, and End-stage (RIFLE) classification.

This classification has been validated by several studies in adults and children (6–13). More recently, the Acute Kidney Injury Network (AKIN) was established, which is a multidisciplinary and intersociety group aimed at improving the care of patients with AKI through the development of uniform standards and classification of the disorder (14,15). A definition based on small changes in SCr and/or urine output within a time frame of 48 hours was proposed. The rationale is to find sensitive and inclusive criteria that consider the relationship between small changes in SCr and mortality, as well as the fact that early detection of kidney injury could prevent or attenuate further damage.

The AKIN definition was proposed as an interim definition/staging system that needs to be validated and, consequently, modified according to emergent evidence (16–20). Some studies compared the AKIN versus the RIFLE definitions (17–19), and others assessed only AKIN definitions (16,20). To date, no

*Instituto Médico de Previsión y Asistencia IMPASA, Montevideo, Uruguay; [†]Hospital Universitario de Getafe, and [‡]Centro de Investigación Biomédica en Red de Enfermedades Respiratorias (CIBERES), Madrid, Spain; [§]Interdepartmental Division of Critical Care Medicine, and Department of Medicine, Division of Respiriology, University Health Network, University of Toronto, Toronto, Ontario, Canada; ^{||}Hospital de Clinicas, Depto de Fisiopatología, Hospital Espanol, Montevideo, Uruguay; [¶]Hospital Profesor A. Posadas, El Palomar, Buenos Aires, Argentina; ^{**}Sanatorio Mitre, Buenos Aires, Argentina; ^{††}Medizinische Hochschule, Hannover, Germany; ^{†††}Clinica Alemana de Santiago, Santiago, Chile; ^{§§}Dokuz Eylul University, Istanbul, Turkey; ^{|||}Clinica Medellín y Universidad Pontificia Bolivariana, Medellín, Colombia; ^{¶¶}Hospital ABC, México DF, Mexico; ^{¶¶¶}Wythenshawe Hospital, Manchester, United Kingdom; ^{††††}Fattouma Bourguiba Monastir, Tunisia; ^{†††††}Hospital Militar de Quito, Ecuador; ^{§§§}King Fahad National Guard Hospital, Riyadh, Saudi Arabia; ^{|||}Hospital de Santo Antonio dos Capuchos, Centro Hospitalar de Lisboa Central, E.P.E., Lisboa, Portugal; ^{¶¶¶}Papageorgiou General Hospital, Thessaloniki, Greece; ^{¶¶¶¶}University of Texas Health Science Center, and South Texas Veterans Health Care System, Audie L. Murphy Hospital, San Antonio, Texas

Correspondence: Dr. Andrés Esteban, Intensive Care Unit, Hospital Universitario de Getafe, Carretera de Toledo Km 12,500, 28905 Getafe, Madrid, Spain. Phone: 34-916834982; Fax: 34-916832095; E-mail: aesteban@ucigetafe.com

study has assessed separately the accuracy of each component of the AKI criteria based on changes in relative or absolute rise in SCr.

On the other hand, it has been shown that not only increases but also reductions in SCr are associated with worse outcomes (21). Hence, the inclusion of a drop in SCr as a diagnostic criterion for AKI has been proposed by some authors (20).

The aim of the present study was to evaluate the two creatinine-based AKIN diagnostic criteria in a large cohort of critically ill patients under mechanical ventilation (MV). The primary end point was in-hospital mortality, and secondary end points were intensive care unit (ICU) and hospital length of stay and duration of MV. As a secondary aim, we assessed the relationship of a negative variation in SCr with hospital mortality.

Patients and Methods

Study Population

The VENTILA Group database was used for this study (22). This is a prospective, observational cohort including 4968 consecutive adult patients who received MV (invasive or noninvasive) for at least 12 hours in 349 ICUs from 23 countries, from March 1, 2004, to March 31, 2004. The Institutional Review Board of each participating institution approved the study protocol. Only patients who were ventilated for 48 hours or more and had at least two determinations of SCr within the first 48 hours of MV were included in the study. Patients with missing SCr values or unknown status at hospital discharge were excluded. The database did not register information on preadmission renal function, urine output, or need of renal replacement therapy. Demographic data (age, simplified acute physiology score [SAPS II], gender, weight, and height) and indication for MV were collected for each patient. Information on ventilator settings, arterial blood gases, SCr, serum bilirubin, platelet count, complications, and organ dysfunction were recorded daily until death, ICU discharge, or day 28, whichever came first. Laboratory tests, including SCr, were performed in each institution. A complete description of the cohort can be found elsewhere (22).

Data Analysis

AKI was diagnosed according to the AKIN criteria by an absolute increase in SCr of ≥ 0.3 mg/dl (>26.4 $\mu\text{mol/L}$) and/or a percentage increase of $\geq 50\%$ (1.5-fold) within the first 48 hours of MV (10). The first SCr determination after starting MV was considered as baseline (SCr_0), over which the AKIN criteria were applied. Day 0 was the day of initiation of MV, with day 1 starting at 8:00 a.m. the next calendar day. The difference of SCr was calculated as the maximum variation of any value of SCr on day 0, day 1, or day 2. The relationship between AKI and several outcomes, including in-hospital mortality, ICU, and hospital length of stay and duration of mechanical ventilation was studied.

For the second aim of the study patients were classified into three groups according to the variation of SCr (ΔSCr) between day 0 and day 1 of MV as follows: group 1 ($\Delta\text{SCr} \leq -0.3$ mg/dl); group 2 (ΔSCr from -0.30 to $+0.29$ mg/dl); and group 3 ($\Delta\text{SCr} \geq +0.3$ mg/dl). One hundred

seventy-five patients with an SCr of 4 mg/dl at day 0 were excluded for the analysis. We selected this time frame because the peak change in SCr occurred in the first 24 hours of MV in the majority of cases and also to avoid confusion resulting from the inclusion of patients with both positive and negative changes in SCr during periods of time longer than 24 hours. Clinical characteristics and mortality rate were analyzed between groups.

Statistical Analyses

Continuous variables are expressed as mean and SD, or median and interquartile range (IQR), and compared using the *t* test and ANOVA or the Mann-Whitney test where appropriate. Categorical variables are expressed as proportions and 95% confidence intervals and were compared by the χ^2 test. Statistical significance was accepted as a two-sided $P < 0.05$. In-hospital mortality was adjusted for prognostic factors by multivariate analysis using a conditional logistic regression model and a forward stepwise selection method correcting for collinearity. Variables that reached a $P < 0.10$ in the univariate model were included in the multivariate model. The statistical package SPSS version 15.0 (Chicago, IL) was used for the analysis.

Results

We studied 2783 patients with at least two determinations of SCr available within the first 48 hours of MV. Baseline characteristics and outcomes of the general population are summarized in Table 1. All-cause ICU mortality rate was 37% and in-hospital mortality was 43% (Table 2). Eighty-three percent of patients were started on MV within the first 24 hours of ICU admission (2222 out of 2669 patients with data on time of initiation of MV).

Eight-hundred three patients (28.8%) fulfilled the AKIN diagnostic criteria according to their change in SCr (absolute and/or relative) over the first 48 hours under MV. Patients with and without AKI showed differences in age, gender, severity of illness, SCr_0 , indication for mechanical ventilation, hospital length of stay, and mortality rate (Table 1 and Table 2). Of the 803 patients, 431 (53.7%) had AKI according to only the absolute criterion (AKI_A), 362 (45.1%) according to both the absolute and the relative criteria (AKI_{R+A}), and the remaining 10 patients according to only the relative criterion. The latter group was not considered for the analysis because of the low number of cases. AKI_A and AKI_{R+A} groups showed no significant differences in clinical characteristics (demographics, reason for MV, and physiologic variables) and mortality (53.6% versus 57.7%, respectively), but they did differ in age (62.9 ± 16.1 versus 57.9 ± 17.4 years, respectively; $P < 0.000$) and SCr_0 (median [IQR]: 2 [1.3 to 3.4] versus 1.1 [0.8 to 1.6], respectively; $P < 0.001$).

We analyzed whether the prevalence of AKI defined by the absolute or by the relative and absolute criteria was related to SCr_0 . The prevalence of AKI was highly dependent on SCr_0 and the diagnostic criteria adopted (Figure 1). As SCr_0 rises, the prevalence of AKI was higher if patients met only the absolute criterion. On the other hand, the prevalence of AKI remained stable over the entire range of SCr_0 if the relative and absolute criteria were met. Of note, no patient met the absolute

Table 1. Clinical characteristics of patients with and without AKI

| | All Cases (2783) | AKI (803) | Non-AKI (1980) | P |
|--|------------------|------------------|------------------|------|
| Age, years, mean (SD) | 59 (17) | 61 (17) | 58 (17) | 0.01 |
| Men, <i>n</i> (%) | 1691 (61) | 513 (64) | 1178 (59) | 0.03 |
| SAPS II, points, median (IQR) | 44 (33 to 56) | 49 (37 to 61) | 42 (32 to 53) | 0.01 |
| SCr ₀ , mg/dl, median (IQR) | 1.1 (0.8 to 1.8) | 1.5 (1.0 to 2.4) | 1.0 (1.0 to 1.6) | 0.01 |
| Main reason for mechanical ventilation, <i>n</i> (%) | | | | |
| chronic obstructive pulmonary disease | 148 (5) | 28 (3) | 120 (6) | 0.01 |
| asthma | 21 (1) | 2 (0.2) | 19 (1) | 0.05 |
| other chronic pulmonary disease | 48 (2) | 8 (1) | 40 (2) | 0.07 |
| coma | 492 (18) | 98 (12) | 394 (20) | 0.01 |
| neuromuscular disease | 34 (1) | 4 (0.5) | 30 (1.5) | 0.03 |
| acute respiratory failure | | | | |
| postoperative | 405 (15) | 146 (18) | 259 (13) | 0.01 |
| pneumonia | 363 (13) | 117 (15) | 246 (12) | 0.13 |
| sepsis | 328 (12) | 116 (14) | 212 (11) | 0.01 |
| trauma | 187 (7) | 33 (4) | 154 (8) | 0.01 |
| congestive heart failure | 160 (6) | 63 (8) | 97 (5) | 0.01 |
| cardiac arrest | 149 (5) | 51 (6) | 98 (5) | 0.13 |
| ARDS | 106 (4) | 32 (4) | 74 (4) | 0.74 |
| aspiration | 89 (3) | 22 (3) | 67 (3) | 0.40 |
| other ARF | 253 (9) | 83 (10) | 170 (9) | 0.14 |

Quantitative data are displayed as median, interquartile range, except for age (mean, SD). Qualitative data, as percentage across rows. Statistical significance was assessed between patients with and without AKI (*t* test for age, Mann–Whitney for SAPS II and SCr₀. AKI, acute kidney injury; ARDS, acute respiratory distress syndrome; ARF, acute renal failure; IQR, interquartile range; SAPS, simplified acute physiology score; SCr₀, serum creatinine at day 0.

Table 2. Outcomes of patients with and without AKI

| | All cases (2783) | AKI (803) | Non-AKI (1980) | P |
|--|------------------|---------------|----------------|------|
| Invasive mechanical ventilation, ^a <i>n</i> (%) | 2669 (96) | 781 (97) | 1888 (95) | 0.02 |
| Days between hospital and ICU admission, mean (SD) | 4.7 (15.0) | 5.6 (17.5) | 4.3 (13.9) | 0.04 |
| Days between ICU admission and mechanical ventilation, mean (SD) | 0.5 (1.9) | 0.6 (2.1) | 0.4 (1.9) | 0.10 |
| Days on mechanical ventilation, median (IQR) | 6 (4 to 10) | 6 (4 to 10) | 5 (4 to 9) | 0.74 |
| ICU length of stay, days, median (IQR) | 10 (6 to 18) | 12 (6 to 20) | 11 (7 to 19) | 0.31 |
| Hospital length of stay, days, (IQR) | 20 (11 to 35) | 19 (10 to 33) | 20 (11 to 35) | 0.03 |
| ICU mortality, <i>n</i> (%) | 1023 (37) | 397 (50) | 626 (32) | 0.01 |
| In-hospital mortality, <i>n</i> (%) | 1207 (43) | 445 (55) | 762 (38) | 0.01 |

Summary data on outcomes, according to the objectives of the study. Time-dependent variables (days on mechanical ventilation, ICU, and hospital length of stay) were considered only in survivors. AKI, acute kidney injury; ICU, intensive care unit; IQR, interquartile range.

^aThere were a few patients receiving only noninvasive mechanical ventilation at study entry, explaining why the percentage of patients in this row is not 100%.

criterion when SCr₀ was lower than 0.60 mg/dl. Thus, meeting simultaneously the relative and absolute criteria improves the accuracy of the definition, regardless of the baseline SCr. AKI was identified as an independent predictor of all-cause in-hospital mortality (odds ratio 1.65, 95% confidence interval 1.23 to 2.14) (Table 3).

Finally, the three groups of Δ SCr showed differences in clinical characteristics and mortality. Considering group 2 as the reference group, patients with a negative Δ SCr (group 1) were older, had higher SCr₀, had worse values of SAPS II, pH, PA/FiO₂, and serum bilirubin, and had a higher mortality rate (Table 4 and Table 5).

Discussion

It has been shown that small increments in SCr are associated with a higher mortality rate, need for RRT, and end-stage renal disease (2,21,23,24). Thus, the Acute Kidney Injury Network recently proposed new definition criteria based on small changes in SCr and/or reduction in urine output. One of the advantages of the AKIN definition is that it requires only two SCr values within 48 hours, eliminating the need for a baseline SCr.

Risk factors for AKI included age, disease severity, and several comorbidities (Table 1). Unlike other studies (2), we did not find that the female gender was associated with

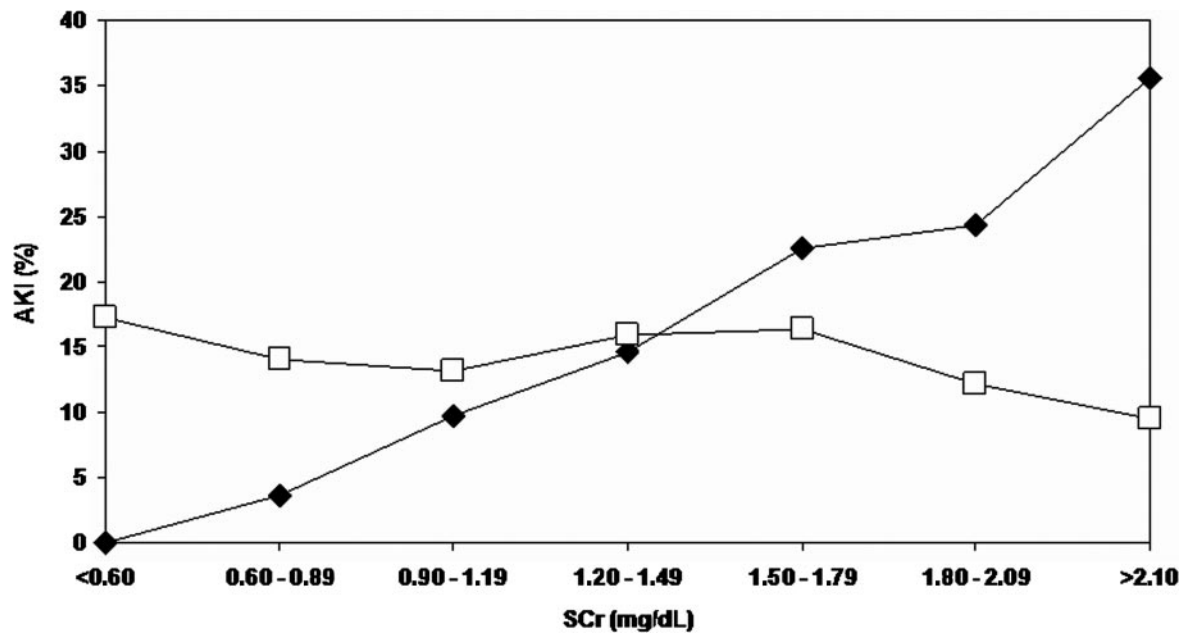


Figure 1. | Prevalence of AKI diagnosed by the absolute criterion (431 patients) or both the relative and the absolute criteria (362 patients). Solid diamonds: absolute criterion. Open squares: relative and absolute criterion. Very few patients met only the relative criterion and thus are not included in the analysis. AKI, acute kidney injury, SCr, serum creatinine concentration.

Table 3. Risk factors for in-hospital mortality according to multivariate analysis

| | Odds ratio | 95% confidence interval | P |
|--------------------------------|-------------------|-------------------------|-------|
| Age | 0.98 ^a | 0.97 to 0.99 | <0.01 |
| SAPS II | 0.98 ^a | 0.97 to 0.99 | <0.01 |
| Serum creatinine at day 0 | 0.93 ^a | 0.86 to 1.01 | 0.07 |
| Serum bilirubin at day 0 | 0.94 ^a | 0.90 to 0.98 | 0.02 |
| Respiratory rate at day 0 | 0.97 ^a | 0.95 to 0.99 | 0.06 |
| PEEP at day 0 | 1.05 ^a | 1.01 to 1.09 | 0.08 |
| Hospital length of stay | 1.03 ^a | 1.02 to 1.03 | <0.01 |
| Days on mechanical ventilation | 0.96 ^a | 0.95 to 0.98 | <0.01 |
| Hemorrhagic stroke | 1.94 | 1.19 to 3.14 | 0.07 |
| Cardiac arrest | 2.53 | 1.42 to 4.53 | 0.02 |
| ARDS | 2.34 | 1.23 to 4.28 | 0.06 |
| Hospital pneumonia | 2.58 | 1.41 to 4.78 | 0.02 |
| Trauma | 0.51 | 0.29 to 0.91 | 0.02 |
| Sepsis | 1.44 | 1.08 to 1.93 | 0.01 |
| AKI | 1.65 | 1.23 to 2.14 | <0.01 |

Only variables that remained in the equation after forward stepwise selection method are displayed. AKI, acute kidney injury; ARDS, acute respiratory distress syndrome; PEEP, positive end expiratory pressure; SAPS, simplified acute physiology score.

^aPer unit of variation: age (years); SAPS II (point); serum creatinine and serum bilirubin (mg/dl); duration of mechanical ventilation and hospital length of stay (days).

mortality, but rather male patients were more likely to develop AKI (Table 1). We cannot explain this discrepancy on the basis of our results.

Our findings support the validity of the new AKIN creatinine-based criteria, either by the absolute or by the relative rise of SCr, because patients with AKI had worse clinical outcomes such as adjusted mortality rate, hospital length of stay, and days on MV (Table 2 and Table 3). In addition to AKI, reasons for MV (hospital pneumonia, acute respiratory distress syndrome, cardiac arrest, hem-

orrhagic stroke, and sepsis) were strongly associated with outcome as is usually reported (22).

We found different prevalence of AKI according to the definition criteria (Figure 1). Eight hundred three of 2783 patients (28.8%) had AKI based on any AKIN criterion (AKI_A or AKI_{R+A} or AKI_R), but the prevalence dropped to 372 (13.4%) if both criteria had to be met (AKI_{R+A}). Moreover, when AKI_A and AKI_{R+A} were analyzed as separate populations, it was found that having to meet both criteria (absolute and relative) was more accurate in patients with

| | Group 1 | Group 2 | Group 3 | P |
|--|---------------|---------------|---------------|-------|
| Age, years, mean (SD) | 60.9 (16.0) | 57.8 (17.7) | 59.7 (16.9) | 0.01 |
| Weight, kg, mean (SD) | 76.4 (21.0) | 76.4 (20.8) | 78.2 (21.6) | <0.01 |
| SAPS II, median (IQR) | 47 (37 to 60) | 42 (32 to 53) | 49 (37 to 64) | <0.01 |
| pH, mean (SD) | 7.34 (0.11) | 7.37 (0.10) | 7.32 (0.13) | 0.01 |
| Pa/FiO ₂ , mean (SD) | 217 (116) | 239 (121) | 201 (114) | 0.01 |
| Serum bilirubin, mg/dl, mean (SD) | 2.41 (4.7) | 1.67 (2.58) | 2.42 (4.33) | 0.01 |
| Serum creatinine, mg/dl, mean (SD) | 1.89 (0.82) | 1.07 (0.59) | 1.58 (0.82) | 0.01 |
| Platelet count, 10 ³ /ml, mean (SD) | 207 (115) | 218 (124) | 177 (115) | <0.01 |

Relevant quantitative parameters were analyzed between the three Δ SCr groups. Laboratory values are from day 0. Patients with SCr \geq 4 mg/dl were excluded from this analysis. IQR, interquartile range; SAPS, simplified acute physiology score.

| | Group 1 (n = 351) | Group 2 (n = 1553) | Group 3 (n = 704) | P |
|--|-------------------|--------------------|-------------------|------|
| Men (n, %) | 218 (62.1) | 904 (57.3) | 457 (64.9) | 0.06 |
| Sepsis (n, %) | 43 (15.0) | 140 (9.0) | 103 (14.6) | 0.01 |
| Trauma (n, %) | 19 (5.4) | 131 (8.4) | 31 (4.4) | 0.01 |
| Cardiac arrest (n, %) | 29 (8.3) | 64 (4.1) | 44 (6.3) | 0.01 |
| DA >15 μ g/kg per min and/or NE >0.1 μ g/kg per min (n, %) | 69 (19.7) | 206 (13.3) | 192 (27.3) | 0.01 |
| In-hospital mortality (n, %) | 147 (41.9) | 569 (36.6) | 393 (55.8) | 0.01 |

Variables are expressed as percentage of patients having the condition: men, sepsis, trauma, cardiac arrest, use of vasoactive drugs during first 24 hours in the ICU, in-hospital mortality. Data were compared by χ^2 between groups 1 and 2. Patients with SCr \geq 4 mg/dl were excluded from this analysis. DA, dopamine; NE, norepinephrine.

low values of SCr₀, whereas meeting only the absolute criterion detected more patients if SCr₀ was higher. The level of SCr at the start of MV in each subset of patients was in accordance with this finding because SCr₀ was higher in AKI_A and lower in AKI_{R+A} patients. These findings bring up the question of whether the AKIN creatinine-based definition and classification system is accurate and independent of the use of a relative or an absolute increase in SCr, and of the baseline renal function.

In a recent publication, Waikar and Bonventre (25) hypothesized that “the percentage change of SCr will significantly delay the diagnosis of AKI in patients with chronic kidney disease because the level of baseline kidney function may influence the kinetics of creatinine rise after an acute injurious event to the kidney.” In fact, on the basis of a simulation model that relies on the basic mass balance principle, the authors demonstrated that percentage changes in SCr are highly dependent on steady state and baseline renal function. Thus, they suggest that AKIN and RIFLE definitions based on a percentage increase of SCr do not perform adequately for the diagnosis of AKI in the presence of chronic kidney disease. An absolute rise of SCr seems to be more appropriate for an early identification of patients with AKI. In line with the proposal of Waikar and Bonventre (25), our findings suggest that the diagnosis criterion based on the percentage increase of SCr could underestimate and/or delay the identification of patients with AKI, particularly when the initial SCr is above normal values. On the other hand, in patients with low values of

SCr, such as the elderly or pregnant women, the relative criterion diagnosis seems to be more accurate.

Another interesting finding of our study was that the subset of patients characterized by a reduction of SCr over the first 24 hours in the ICU showed a higher mortality rate than those showing no change in SCr (Table 4 and Table 5). These patients were similar to patients with AKI (group 3) in terms of age, gender, SAPS II, and percentage of patients with sepsis, trauma, cardiac arrest, hemodynamic failure, and some physiologic variables at the beginning of MV (pH, plateau pressure, and serum bilirubin). Interestingly, SCr₀ in group 1 was the highest, when compared with those of groups 2 and 3.

We have no satisfactory explanation for the finding of a high mortality rate in patients showing a decrease in SCr. It could be hypothesized that these patients were captured in the recovery phase of a previously existing AKI at the start of MV. This is actually likely according to the study design, as patients were included in the database not at the time of ICU admission but at the time of the initiation of MV. To minimize this effect, we excluded from this analysis (Table 4 and Table 5) patients with SCr \geq 4 mg/dl. Also, it is reasonable to think that SCr could drop because of hemodilution secondary to fluid administration, which is likely, considering the severity of illness of these patients. Little attention has been paid to this point in the literature. Lassnigg *et al.* were the first to describe the association of a negative variation in SCr with mortality in cardiac surgery patients (21) and this finding was con-

firmed in a later study by the same group (26). This relationship was mentioned also by other investigators such as Ostermann *et al.* (20) who included the reduction in SCr value in the definition of AKI. Future prospective studies should confirm this finding.

Our study has some limitations. First, as the original database was designed to look at mechanically ventilated patients, we had to set the initial time point of the current study in the moment of initiation of MV. This could have led in our study to an underestimation of the true incidence of AKI. We think, however, that the effect of choosing the time of initiation of MV, rather than the time of ICU admission, as the initial reference point in time is probably not very important for estimating the incidence of AKI, as most patients (83%) started to receive MV within 24 hours of ICU admission. Second, some important information, such as urine output, baseline SCr, the characteristics of fluid resuscitation, or need of RRT was lacking in the database. Third, the database contains information from self-appointed ICUs that may not be representative of the practice in the different geographical regions. Fourth, in this multicenter multinational study, local laboratories made different determinations, and information on the specific laboratory method used was not captured in the database. Therefore, the results reported could be biased because of intragroup or intergroup variability. The large sample size studied could minimize this bias. Fifth, missing data on previous renal function, RRT, and other variables (*e.g.*, fluid challenge, hemodilution, and drug interaction) hinder the proposal of a plausible explanation for the relationship between a negative Δ SCr and outcome.

Among the strengths of the study, we can mention the large sample size, with patients from many different geographical regions, making it reasonable to assume that indeed they may be representative of critically ill patients from different areas of the world. Second, the design of the study allowed us to test separately both components of the creatinine-based definition, confirming the accuracy of the definition provided that each component was applied in relation to the initial SCr. Third, we provide evidence to support the emerging concept of the relationship between a negative variation of SCr and mortality in mechanically ventilated patients.

Acknowledgments

This study was supported by CIBERES from Instituto de Salud Carlos III, Spain. The study sponsor had no role in study design, in the collection, analysis, and interpretation of data; in the writing of the report, nor in the decision to submit the paper for publication.

The VENTILA group members include the following:

Argentina: *Coordinators:* Carlos Apezteguia (Hospital Prof. A. Posadas, El Palomar, Buenos Aires) and Pablo Desmery (Sanatorio Mitre, Buenos Aires). *Other members:* A. Sarasino and D. Ceraso (Hospital Dr. Juan A. Fernandez, Buenos Aires), D. Pezzola and F. Villarejo (Hospital Prof. A. Posadas, El Palomar), C. Cozzani and M. Torres Boden (Hospital Dr. C. Argerich, Buenos Aires), C. Santos and E. Capparelli (Hospital Eva Peron, San Martín), M. Tavella and C. Irrazabal (Hospital de Clínicas Jose de San Martín, Buenos Aires), L. Cardonnet and A. Diez (Hospital Provincial del Centenario, Rosario), A. Giannelli and L. Vargas (Policlinico de

Neuquen), M. Bustamante (Hospital Heroes de Malvinas, Merlo), E. Turchetto (Hospital Privado de la Comunidad, Mar del Plata), J. Teves and O. Elefante (Hospital Oscar Alende, Mar del Plata), C. Sola and J. Mele (Hospital Dr. Jose Penna, Bahia Blanca), V. Sciuto and P. Grana (Hospital Provincial de Neuquen), G. Jannello and R. Valentini (CEMIC, Buenos Aires), S. Ilutovich (Sanatorio Mitre, Buenos Aires), L. Huespe Gardel (Hospital Escuela Jose F. de San Martín, Corrientes), J. Scapellato and E. Orsini (Hospital F. Santojanni, Buenos Aires), G. Aguero and A. Sanchez (Policlinico Regional J. Peron, Mercedes), R. Fernandez and L. Villalobos Castaneda (Hospital Italiano, Buenos Aires), F. Gonzalez and E. Estenssoro (Hospital General San Martín, La Plata), S. Lasdica (Hospital Privado del Sur, Bahia Blanca), A. Gómez and J. Scapellato (Clinica de la Esperanza, Buenos Aires), P. Pratesi (Hospital Universitario Austral, Pilar), M. Blasco and F. Villarejo (Clínica Olivos, Olivos), G. Olarte and C. Bevilacqua (Clínica Modelo de Moron/Hospital San Juan de Dios, R. Mejia), M. Quinteros (Sanatorio San Lucas, San Isidro), P. Ripoll (Clinica La Sagrada Familia, Buenos Aires), S. Filippus (Clinica del Valle, Comodoro Rivadavia), F. Guzman Diaz and M. Deheza (Hospital B. Rivadavia, Buenos Aires), E. Garcia and J. Arrieta (Hospital Regional de Comodoro Rivadavia), P. Pardo and J. Neira (Sanatorio de la Trinidad, Buenos Aires), J. Nunez and F. Pálizas (Clinica Bazterrica, Buenos Aires), A. Ciccolini and G. Murias (Sanatorio Santa Isabel, Buenos Aires), W. Vazquez and M. Grilli (Hospital Espanol, Mendoza), F. Chertcoff and E. Soloaga (Hospital Británico, Buenos Aires), D. Vargas and J. Beron (Hospital Pablo Soria, San Salvador de Jujuy), A. Maceira and P. Schoon (Hospital Prof. Luis Guemes, Haedo), D. Pina (Sanatorio Franchín, Buenos Aires), E. Sobrino and A. Raimondi (Sanatorio Mater Dei, Buenos Aires), E. De Vito (Instituto Alfredo Lanari, Buenos Aires).

Belgium: M. Malbrain (Ziekenhuis Netwerk, Antwerpen).

Bolivia: *Coordinator:* Freddy Sandi Lora (Hospital obrero N° 1, La Paz). *Other members:* A. Lavandez and C. Alfaro (Complejo Hospitalario Viedma, LA Paz), J. Guerra (Instituto gastroenterologico boliviano japonés, Santa Cruz).

Canada: *Coordinators:* Niall D. Ferguson (Toronto Hospital Western) and Maureen O. Meade (McMaster University). *Other members:* J.T. Granton (Toronto General Hospital), S.E. Lapinsky (Mount Sinai Hospital, Toronto), J. Meyer (St. Joseph's Hospital, Toronto), D.C. Scales (St. Michael's Hospital, Toronto), R.A. Fowler (Sunnybrook Health Sciences Centre, Toronto, ON), B. Kashin (William Osler Health Centre, Brampton, ON), D.J. Cook (St. Joseph's Healthcare).

Chile: *Coordinator:* Vinko Tomicic (Clinica Alemana de Santiago). *Other members:* L. Soto (Instituto Nacional del Torax, Santiago), C. Romero (Hospital Clinico Pontificia Universidad Catolica, Santiago), M. Teresa Caballero and L. Chiang (Hospital naval almirante NEF), E. Poch (Instituto de Neurocirugia), J. Canteros Gatica (Hospital Curico), H. Ugarte (Hospital de Coquimbo), M. Calvo, C. Vargas, and M. Yacsich (Hospital Regional de Valdivia), E. Tobar (Hospital Clinico de la Universidad de Chile, Santiago), J.G. Urra (Clinica Alemana de Temuco).

Colombia: *Coordinator:* Marco A. Gonzalez (Clínica Medellin y Universidad Pontificia Bolivariana, Medellin). *Other members:* A. Guerra (Hospital General de Medellin and Clinica SOMA, Medellin), C. Cadavid (Hospital Pablo Tobon Uribe, Medellin), R. Panesso (Clinica Las Americas, Medellin), M. Granados (Clínica Valle del Lilli, Cali), C. Duenas (Hospital Bocagrande, Cartagena), F. Molina (Clinica Bolivariana, Medellin), R. Camargo (Clinica Gen-

eral del Norte de Barranquilla), G. Ortiz (Hospital de Santa Clara, Bogotá), M. Gomez (Hospital de San Jose).

Ecuador: *Coordinator:* Manuel Jibaja (Hospital Militar de Quito). *Other members:* G. Paredes and E. Bazantes (Hospital Enrique Garces, Quito), P. Jimenez (Hospital Carlos Andrade Martin, Quito), J. Vergara and L. González (Hospital Luis Vernaza Valdez, Guayaquil).

France: *Coordinators:* Laurent Brochard (Centre hospitalier Albert-Chenvier-Henri Mondor, Paris) and Arnaud Thille (Centre hospitalier Albert-Chenvier-Henri Mondor, Paris). *Other members:* L. Mallet (Centre Hospitalier D'Auch), P. Andrivet (Centre Médico-Chirurgical de Bligny, Bris-sous-Forges), O. Peyrouset (Hopital Ambroise Pare, Boulogne Billancourt), I. Mohammedi (Hopital Edouard Herriot, Lyon), E. Guerot (Hopital Europeen Georges Pompidou, Paris), N. Deye (Hopital Lariboisiere, Paris), S. Monsel and F. Bouvet (Hopital Pitie Salpetriere, Paris), M. Darmon (Hopital Saint Louis, Paris), M. Fartoukh and A. Harb (Hopital Tenon, Paris), N. Anguel (Hopital de Bicetre, Kremlin-Bicetre).

Germany: *Coordinator:* Konstantinos Raymondos (Medizinische Hochschule Hannover). *Other members:* A. Nowak, T. Pahlitzsch, and K.F. Rothe (Krankenhaus Dresden-Friedrichstadt), M. Ragaller and T. Koch (Universitaetsklinikum Carl Gustav Carus Dresden), G. Sterzel (Kreiskrankenhaus Loebau, Ebersbach), R. Wittich (Carl-Thiem-Klinikum Cottbus gGmbH), K. Rudolph and J. Raumanns (St. Elisabeth gGmbH Leipzig), U. Grueneisen and F. Stupacher (Bundeswehrkrankenhaus Leipzig), H. Bromber, G. Leonhardt, and J. Soukup (Universitaetsklinikum der Martin-Luther-Universitaet Halle-Wittenberg), C. Wuttke (Krankenhaus St. Elisabeth und St. Barbara Halle, Saale), M. Holler (Staedtisches Krankenhaus Martha-Maria Halle-Doelau gGmbH), J. Haberkorn (Georgius-Agricola-Klinikum Zeitz), P. Jehle (Paul-Gerhard-Stiftung, Lutherstadt Wittenberg), B. Albrecht (Zeisigwaldklinik Bethanien Chemnitz), Klut (Kreiskrankenhaus Rochlitz), H.J. Hartung (Vivantes Krankenhaus am Urban, Berlin-Kreuzberg), H. Gerlach (Vivantes-Klinikum Neukoelln, Berlin), T. Henneberg, S. Weber-Carstens, K. Haid, and C. Melzer-Gartzke, M. Oppert (Charité Universitaetsklinikum, Campus Virchow, Berlin), M. Refenberg (Lungenklinik Heckeshorn, Berlin), Ch. Werel and A. Kopietz (Klinikum Barnim GmbH, Werner Forßmann Krankenhaus, Eberswalde), T. Nippasch and D. Hoffmeister (Ruppiner Klinikum GmbH, Neuruppin), M. Schneider (Dietrich-Bonhoeffer-Klinikum-Neubrandenburg), D.A. Vagts and G. Noeldge-Schomburg (Medizinische Fakultät der Universitaet Rostock), G. Savinski and T. Kloess (Allgemeines Krankenhaus Harburg, Hamburg), C. Frenkel, D. Yakisan, H. Schroeder, and C. Daniels (Staedtisches Klinikum Lueneburg), B. Sedemund-Adib (Universitaetsklinikum Schleswig Holstein-Campus Luebeck), S. Krueper (Klinikum Hannover Nordstadt), J. Ahrens, U. Molitoris, and K. Johanning (Medizinische Hochschule Hannover), D. Korth and W. Seitz (Kreiskrankenhaus Hameln), J. Kleideiter and P. Palomino (Staedtische Kliniken Bielefeld gGmbH), A. Lunkeit and Schlechtweg (Klinikum Bad Salzung gGmbH), M. Quintel (Universitaetsklinikum der Georg-August-Universitaet Goettingen), Schild and C.P. Crieé (Evangelisches Krankenhaus Goettingen-Weende e.V., Bovenden-Lenglern), M. Bund (Albert-Schweitzer-Krankenhaus Northeim), M. Hundt, U. Schulze, and J. Kolle (Kreiskrankenhaus Charlottenstift, Stadtoldendorf), J. Offensand, S. Youssef, and J.P. Juvana (Klinikum Salzgitter GMBH), W. Seyde (Staedtisches Klinikum Wolfenbuettel), T. Luecke and A. Gruener (Universitaetsklinikum Mannheim), E. Calzia (Universitaetsklinikum fur Anesthesiologie, Ulm), J. Heine, M. Borth, U. von Leitner, and M. Hoffmann (Dr.

Herbert-Nieper-Krankenhaus-Goslar), W. Brandt (Universitaetsklinikum Magdeburg), A. Keller and S. Scieszka (Krankenhaus Neuwerk, Moenchengladbach), E. Schroeder and F.L. Deres (Kreiskrankenhaus Dormagen), M. Burcher, T. Bernhardt, and W. Wilhelm (St.-Marien-Hospital, Luenen), M. Beiderlinden (Universitaetsklinikum Essen), H. Steiniger and V. Weißkopf (Ruhlandklinik, Essen), H. Militzer (Evangelisches und Johanniter Klinikum, Dinslaken), K. Eicker and F. Hinder (Universitaetsklinikum Muenster), C. Weillach and M. Raab (St. Josefs-Stift Cloppenburg), Ragaymutu (Kliniken der Stadt Koeln Krankenhaus Holweide), T. Moellhoff and K. Tsompanidis (Katholische Stiftung Marienhospital Aachen), D. Henzler and R. Kuhlen (Universitaetsklinikum Aachen), H. Wrigge, C. Putensen, and F.L. Dumoulin (Universitaetsklinikum Bonn), M. Foedisch and J. Busch (Evangelisches Waldkrankenhaus Bad Godesberg gGmbH, Bonn), W. Theelen (St. Johannes-Krankenhaus Troisdorf), A. Deller (Krankenhaus der Barmherzigen Brueder, Trier), W. Baier (St. Nikolaus-Stiftshospital GmbH, Andernach), Eller (Staedt. Hellmig-Krankenhaus, Kamen), K. Schwarke (Evang Krankenhaus Schwerte GmbH), Buettner (Evangelisches Krankenhaus Elisabethenstift gGmbH, Darmstadt), K.P. Wresch and K. Steidel (St.-Vincentius-Krankenhaus Speyer), J.F. Meyer (Universitaetsklinikum der Ruprecht-Karls-Universitaet Heidelberg), M. Layer (Thoraxklinik Heidelberg gGmbH), G. Meinhardt (Robert-Bosch-Krankenhaus, Stuttgart), J. Fritschi and P. Zaar (Ermstallklinik Staedtisches Krankenhaus Sindelfingen), H.P. Stegbauer (Kreiskrankenhaus Leonberg), Tumbass and S. Hahn (Ermstallklinik Bad Urach), H. Mende, M. Fischer, J. Martin, and A. Assmann (Klinik am Eichert Goepfingen), V. Schoeffel, K. van Deyk, and S. Seyboth (Stadtklinik Baden-Baden), H. Kerger and Ernst (Evangelisches Diakoniekrankenhaus, Freiburg), H.F. Ginz (Kreiskrankenhaus Loerrach), F. Brettner (Krankenhaus der Barmherzigen Brueder, Muenchen), O. Karg (ASKLEPIOS Fachkliniken Muenchen-Gauting), M. Glaser and T.P. Zucker (Klinikum Traunstein), J. Jahn and A. Schneider (Fachkliniken Wangen), M. Burkert (Bundeswehrkrankenhaus Ulm), H. Kuenzig and T. Bein (Klinikum der Universitaet Regensburg), A. Speicher (Krankenhaus der Barmherzigen Brueder, Regensburg), J. Brederlau, E. Kaufmann, F. Schuster, and C. Soellmann (Universitaetsklinik Wuerzburg), S. Frenzel and L. Pfeiffer (Unstrut-Hainich Kreiskrankenhaus Muehlhausen), S. Weber-Carstens, K. Haid, C. Melzer-Gartzke, C. von Heymann, and B. Temmesfeld (Charité Universitaetsklinikum, Campus Mitte, Berlin).

Greece: *Coordinator:* Dimitrios Matamis (Papageorgiou General Hospital, Thessaloniki). *Other members:* H. Mouloudi (Ippokration General Hospital, Athens).

Italy: *Coordinator:* Paolo Pelosi (Ospedale di Circolo di Varese). *Other members:* A. Pesenti and N. Rossi (Ospedale San Gerardo, Monza), D. Chiumello and L. Gattinoni (Ospedale Maggiore Policlinico, Milano), P. Severgnini (Ospedale di Circolo di Varese), R. Fumagalli and A. Nikiforov (Ospedali Riuniti di Bergamo), S. Grasso (Ospedale di Venere, Bari).

Mexico: *Coordinator:* José Elizalde (Hospital ABC, México DF). *Other members:* P. Cerda (Centro Médico de las Américas, Mérida), R. Mercado (Hospital Universitario de Monterrey), J. Albe. Castañón (Instituto mexicano del seguro social HECMNS XXI, México DF).

Netherlands: Michael Kuiper (Medical Center Leeuwarden), P.H.M. Egbers and M. Koopmans (Medical Center Leeuwarden).

Peru: *Coordinator:* Ana Maria Montanez Mendoza (Hospital Edgardo Rebagliati Martins, Lima). *Other members:* M. Contardo, J. Cerna, and R. Roldan (Hospital Edgardo Rebagliati Martins,

Lima), J. Zevallos and S. Alcabes (Hospital Guillermo Almenara Irgoyen, Lima), C. Salcedo and D. Bruzone (Hospital Nacional Daniel Alcides Carrion, Callao), J. Quinones (Hospital de Emergencias Grau, Lima), M. Suarez Lazo (Hospital Nacional Hipolito Unanue, Lima), A. Cifuentes (Hospital de Emergencias Jose Casimiro Ulloa, Lima), M. Mayorga (Clinica San Pablo, Lima).

Portugal: *Coordinator:* Rui Moreno (Hospital de Santo Antonio dos Capuchos, Lisboa). *Other members:* P. Casanova (Hospital da Universidade de Coimbra), R. Matos and A.L. Jardim (Hospital de Santo Antonio dos Capuchos, UCIP, Lisboa), A. Godinho (Hospital dos SAMS, UCI, Lisboa), P. Povoia (Hospital Sao Francisco Xavier, UCIM, Lisboa), P. Coutinho (Centro Hospitalar de Coimbra), L. Reis (Hospital de Sao Jose, Unidade de Urgencia Medica, Lisboa).

Saudi Arabia: *Coordinator:* Yaseen Arabi (King Fahad National Guard Hospital). *Other members:* N. Abouchala (King Faisal Hospital), F. Hameed (King Khalid National Guard Hospital).

Spain: *Coordinators:* Nicolas Nin and Eva Tejerina (Hospital Universitario de Getafe). *Other members:* F. Gordo (Fundacion Hospital de Alcorcon), R. Fernandez (Complejo Hospitalario Parc Tauli, Sabadell), R. de Pablo (Hospital Universitario Principe de Asturias, Alcala de Henares), J. Ibanez (Hospital Son Dureta, Palma de Mallorca), E. Fernandez Mondejar (Hospital Virgen de las Nieves, Granada), F. del Nogal (Hospital Severo Ochoa, Leganes), F. Taboada (Hospital Central de Asturias, Oviedo), A. Garcia Jimenez (Hospital Arquitecto Marcide, El Ferrol), Ll. Cabre and J. Morillas (Hospital de Barcelona-SCIAS), S. Macias (Hospital General de Segovia), R. de Celis (Hospital de Galdakao), J. M. Anon (Hospital Virgen de la Luz, Cuenca), P. Ugarte (Hospital Marques de Valdecilla, Santander), T. Mut (Hospital de la Plana, Vila-Real), J. Diarte (Complejo Hospitalario de Ciudad Real), V. Sagredo (Hospital Clinico de Salamanca), M. Valledor (Hospital San Agustin, Aviles), G. Gonzalez and L. Rodriguez (Hospital Morales Meseguer, Murcia), V. Parra and E. Gomez (Hospital de Sagunto), F. Jara (Hospital Mutua de Terrassa), J.M. Quiroga (Hospital de Cabuenes, Gijon), L. Arnaiz (Hospital Clinico Universitario de San Carlos, Madrid), A. Ayensa (Hospital Virgen de la Salud, Toledo), F. Suarez Sippman (Fundacion Jimenez Diaz), F. Carrizosa (Hospital General de Jerez de la Frontera), J.A. Rodriguez Sarria (Hospital de Elda), C. Homs (Hospital San Jorge, Huesca), A. Diaz Lamas (Hospital Cristal Pinor, Ourense), M. Leon (Hospital Arnau de Vilanova, Lleida), J. Allegue (Hospital Nuestra Senora del Rosell, Cartagena), M. Ruano (Hospital La Fe, Valencia).

Tunisia: *Coordinator:* Fekri Abroug (Fattouma Bourguiba, Monastir). *Other members:* M. Besbes, J. Ben Khelil, K. Belkhouja, and K. BenRomdhane (Hospital Abderrahmane Mami, Ariana), S. Ben Lakhal, S. Abdellatif, and K. Bousselmi (Hospital Rabta, Tunis), M. Amamou and H. Thabet (CAMUR, Tunis), L. Besbes and N. Nciri (Fattouma Bourguiba, Monastir), M. Bouaziz, H. Kallel, and M. Bahloul (Habib Bourguiba Sfax), S. ElAtrous, S.Merghli, and M. Feki Hassen (Tahar Sfar Mahdia).

Turkey: *Coordinator:* Nahit Cakar (Dokuz Eylul University, Istanbul). *Other members:* R. Iscimen (Uludag University School of Medicine, Bursa), M. Kyzylkaya (College of Medicine, Ataturk University, Erzurum), B. Yelken (Osmangazi University, Eskisemir), I. Kati (Medical Faculty of Yuzuncu Yil University, Van), T. Guldem (Haydarpasa Numune Teaching and Research Hospital, Istanbul), U. Koca (Dokuz Eylul University, Istanbul), M. Cicek (Inonu University of Medical Faculty, Malatya).

United Kingdom: *Coordinator:* Peter Nightingale (Wythenshawe Hospital, Manchester). *Other members:* J. Hunter (Macclesfield Dis-

trict General Hospital, Macclesfield), J. Hunter (Rotherham District General Hospital, Rotherham), S. Mousdale (Blackburn Royal Infirmary, Blackburn), J. Harper (Royal Liverpool University Hospital, Liverpool), A. Conn (Wansbeck General Hospital, Ashington), D. Higgins (Southend Hospital, Westcliffe-on-Sea), D. Jayson (Southport & Formby District General Hospital, Southport), D. Hawkins (North Staffordshire Hospital, Stoke on Trent).

United States: *Coordinator:* Antonio Anzueto (University of Texas Health Science Center, San Antonio, TX). *Other members:* A.C. Arroliga (The Cleveland Clinic, Cleveland, OH), O. Gajic, Ch. Burger, and L. Gambino (Mayo Clinic, Rochester, MN), D. Ost, A. Fein, A. Kyprianou, L. Shulman, and S. Chang (North Shore University Hospital, Manhasset, NY), J.S. Steingrub, M.A. Tidswell, and K. Kozikowski (Baystate Medical Center, Springfield, MA), C.A. Piquette and L. Morrow (Creighton University Medical Center, Omaha, NE), P. Scheinberg and J. Green (Saint Joseph's Hospital, Atlanta), L. Penogreen and K. Kannady (Georgia State University Kennestone, Atlanta), M. Moss, M. Mealer, and R.D. Restrepo (Grady Hospital Georgia, Atlanta), H.E. Fessler, R. Brower, D. Hager, and A. Scully (Johns Hopkins University Hospital, Baltimore, MD), J. Beamis, D.E. Craven, and W. Miner (Lahay Clinic Medical Center, Burlington, MA), S. Blosser, K. Miller, L. Cornman, and J. Breidinger (Penn State Hershey Medical Center, Hershey, PA), J.T. Huggins and Ch. Strange (Medical University of South Carolina, Charleston, SC), N.S. Hill and L. Lawler (Tufts-North England Medical Center, Boston), M. Rembert (Newark Beth Israel Medical Center, Newark, NJ), H.K. Donnelly, J.D. D'Amico, R.G. Wunderink, N. Quesada, and J. Topin (Northwestern Memorial Home Health University, Chicago), G.T. Kinasewitz and G.L. Lee (University of Oklahoma Health Sciences Center, Oklahoma City, OK), J. Walls and V. Zimmer (Presbyterian Healthcare, Charlotte, NC), A.X. Freire (Regional Medical Center, Memphis, TN), C. Steven and L. Caskey (Louisiana State University Health Sciences Center, Shreveport, LA), R. Dhand and L.A. Despina (University Hospital and Clinics MU Healthcare, Columbia, MO), R. Hyzy, R.E. Dechert, Carl Haas, and D. Fickle (University of Michigan Medical Center, Ann Arbor, MI), D. Marks and S. Benslimane (University of Texas Health Science Center, San Antonio, TX), V.J. Cardenas, Jr. (University of Texas Medical Branch at Galveston, Galveston, TX), M.J. Wing and P. Krumpke (VA Sierra Nevada Health Care System, Reno, NV), J. Truwit and M. Marshall (University of Virginia Health System, Charlottesville, VA), D.L. Herr (Washington Hospital Center, Washington, DC), R.D. Hite (Wake Forest Baptist Hospital Medical Center, Winston-Salem, NC), P.J. McShane and K.N. Olivier (Wilford Hall Medical Center, Lackland Air Force Base, TX), K.W. Presberg (Froedtert & Medical College, Milwaukee).

Uruguay: *Coordinator:* Javier Hurtado (Cudam Sanatorio Colon, Sanatorio IMPASA and Hospital de Clinicas, Montevideo). *Other members:* M. Borde, E. Echavarría, S. Gomez, and M. Beron (Hospital Maciel, Montevideo), F. Villalba (Sanatorio Casa de Galicia, Montevideo), I. Porras (Sanatorio CASMU 2, Montevideo), P. Cardinal, C. Surraco, and V. Navarrete (Sanatorio CASMU 4, Montevideo), F. Rodriguez and J.C. Bagattini (Hospital Britanico, Montevideo), R. Garrido (Hospital Evangelico and Sanatorio IMPASA, Montevideo), S. Infanzon and J. Caraballo (Hospital Militar and CTISMI, Montevideo), C. Santos and A. Garcia (Hospital de Clinicas, Montevideo), R. Cal (CTI-SMI, Montevideo), G. Pittini and J. Cabrera (Centro Nacional de Quemados, Montevideo), F. Bazzano and F. Dominguez (Hospital Pasteur, Colonia), P. Alzugaray, D. Gonzalez, and M. Machado (Sanatorio CAMOC, Carmelo), F.

Torres (Sanatorio Mautone and Asistencial Medica de Maldonado, Maldonado), S. Mareque, M. Korintan, F. Mora, E. Altieri, E. Gianoni, C. Fregosi, A. Crossi, and G. Larrarte (Sanatorio CAAMS, Soriano), O. Pereira (Sanatorio COMTA, Tacuarembó), J. Baraibar (Hospital Regional de Tacuarembó, Tacuarembó), A. Soler (Sanatorio COMEPA, Paysandu), M. Rodríguez Verde (Hospital Paysandu), M. Díaz (Hospital de Salto and Sanatorio Uruguay, Salto), J. Martínez Ramos (Sanatorio Uruguay, Salto), I. Iturralde, W. Gonzalez, and E. Cubas (Sanatorio CAMDEL, Minas), A. Cataldo (Sanatorio CAMEDUR, Durazno), O. Rocha (Sanatorio GREMEDA, Artigas), A. Deicas (Sanatorio CASMU 2 and Sanatorio CASMU 4).

Venezuela: *Coordinator:* Gabriel D'Empaire (Hospital de Clínicas, Caracas). *Other members:* R. Zerpa (Hospital Militar de Caracas, Caracas), M. Narvez (Hospital Domingo Luciani, Caracas), F. Perez (Hospital de Clínicas, Caracas), J. Espana (Hospital Universitario de Caracas, Caracas).

Disclosures

None.

References

- Liaño F, Junco E, Pascual J, Madero R, Verde E, and the Madrid Acute Renal Failure Study Group. The spectrum of acute renal failure in the intensive care unit compared with that seen in other settings. *Kidney Int* 53: 16–24, 1998
- Chertow GM, Burdick E, Honour M, Bonventre JV, Bates DW: Acute kidney injury, mortality, length of stay, and costs in hospitalized patients. *J Am Soc Nephrol* 16: 3365–3370, 2005
- Ishani A, Xue JL, Himmelfarb J, Eggers PW, Kimmel PL, Molitoris BA, Collins AJ: Acute kidney injury increases risk of ESRD among elderly. *J Am Soc Nephrol* 20: 223–228, 2009
- Mehta RL, Chertow GM: Acute renal failure definitions and classification: Time for change? *J Am Soc Nephrol* 14: 2178–2187, 2003
- Bellomo R, Ronco C, Kellum JA, Mehta RL, Palevsky P, and the ADQI Group. Acute renal failure-Definition, outcome measures, animal models, fluid therapy and information technology needs: The Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. *Crit Care* 8: R204–R212, 2004
- Abosaif NY, Tolba YT, Heap M, Russell J, El Nahas AM: The outcome of acute renal failure in the intensive care unit according to RIFLE: Model application, sensitivity, and predictability. *Am J Kidney Dis* 46: 1038–1048, 2005
- Hoste EJA, Clermont G, Kersten A, Venkataraman R, Angus DC, De Baquer D, Kellum JA. RIFLE criteria for acute kidney injury in critically ill patients: A cohort analysis. *Crit Care* 10: R73, 2006
- Ostermann M, Chang RWS: Acute kidney injury in the intensive care unit according to RIFLE. *Crit Care Med* 35: 1837–1843, 2007
- Uchino S, Bellomo R, Goldsmith D, Bates S, Ronco C: An assessment of the RIFLE criteria for acute renal failure in hospitalized patients. *Crit Care Med* 34: 1913–1917, 2006
- Ackan-Adikan A, Zapitelli M, Loffis LL, Washburn KK, Jefferson LS, Goldstein SL: Modified RIFLE criteria in critically ill children with acute kidney injury. *Kidney Int* 71: 1028–1035, 2007
- Ricci Z, Cruz D, Ronco C: The RIFLE criteria and mortality in acute kidney injury: A systematic review. *Kidney Int* 73: 538–546, 2008
- Endre Z, Pickering JW: Outcome definitions in non-dialysis intervention and prevention trials in acute kidney injury (AKI). *Nephrol Dial Transpl* 25: 9–11, 2010
- Cruz D, Ricci Z, Ronco C. Clinical review: RIFLE and AKIN – time for reappraisal. *Crit Care* 13: 211, 2009
- Mehta RL, Kellum JA, Shah SV, Molitoris BA, Ronco C, Warnock DG, Levin A. Acute Kidney Injury Network (AKIN): Report of an initiative to improve outcomes. *Crit Care* 11: R31, 2007
- Murray PT, Devarajan P, Levey AS, Eckardt KU, Bonventre JV, Lombardi R, Herget-Rosenthal S, Levin A: A framework and key research questions in AKI diagnosis and staging in different environments. *Clin J Am Soc Nephrol* 3: 864–868, 2008
- Barrantes F, Tian J, Vazquez R, Amoateng-Adjepong Y, Malhotra CA: Acute kidney injury criteria predict outcome of critically ill patients. *Crit Care Med* 36: 1397–1403, 2008
- Bagshaw SM, George C, Bellomo R, for the ANZICS Database Management Committee. A comparison of the RIFLE and AKIN criteria for acute kidney injury in critically ill patients. *Nephrol Dial Transpl* 23: 1569–1574, 2008
- Lopes JA, Fernandez P, Jorge S, Gonçalves S, Alvarez A, Costa e Silva Z, França C, Martins Prata M. Acute kidney injury in intensive care unit patients: A comparison between the RIFLE and de Acute Kidney Injury Network classification. *Crit Care* 12: R110, 2008
- Joannidis M, Metnitz B, Bauer P, Schusterschitz N, Moreno R, Druml W, Metnitz PG: Acute kidney injury in critically ill patients classified by AKIN versus RIFLE using the SAPS 3 database. *Intensive Care Med* 35: 1692–1702, 2009
- Ostermann M, Chang R, and the Riyadh ICCU Program Users Group. Correlations between the AKI classification and outcome. *Crit Care* 12: R144, 2008
- Lassnigg A, Schmidlin D, Mouhieddine M, Bachmann LM, Druml W, Bauer P: Minimal changes of serum creatinine predict prognosis in patients after cardiothoracic surgery: A prospective cohort study. *J Am Soc Nephrol* 15: 1597–1605, 2004
- Esteban A, Anzueto A, Frutos F, Alia I, Brochard L, Stewart TE, Benito S, Epstein SK, Apezteguia C, Nightingale P, Arroliga AC, Tobin MJ, for the Mechanical Ventilation International Study Group. Characteristics and outcomes in adult patients receiving mechanical ventilation: A 28-day international study. *JAMA* 287: 345–355, 2002
- Levy EM, Viscoli CM, Horwitz RI. The effect of acute renal failure on mortality. A cohort analysis. *JAMA* 275: 1489–1494, 1999
- Nin N, Lombardi R, Frutos-Vivar F, Esteban A, Lorente JA, Ferguson ND, Hurtado J, Apezteguia C, Brochard L, Schortgen F, Raymonds K, Tomacic V, Soto L, González M, Nightingale P, Abrog F, Pelosi P, Arabi Y, Moreno R, Anzueto A; for the VENTILA Group. Early and small changes in serum creatinine concentration are associated to mortality in mechanically ventilated patients. *Shock* 34: 109–111, 2010
- Waikar SS, Bonventre JV: Creatinine kinetics and the definition of acute kidney injury. *J Am Soc Nephrol* 20: 672–679, 2009
- Lassnigg A, Schmid ER, Hiesmayr M, Falk C, Druml W, Bauer P, Schmidlin D: Impact of minimal increases in serum creatinine on outcome in patients after cardiothoracic surgery: Do we have to revise current definitions of acute renal failure? *Crit Care Med* 36: 1129–1137, 2008

Received: October 26, 2010 **Accepted:** March 24, 2011

Published online ahead of print. Publication date available at www.cjasn.org.