RIFLE-Based Data Collection/Management System Applied to a Prospective Cohort Multicenter Italian Study on the Epidemiology of Acute Kidney Injury in the Intensive Care Unit

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Key Words

Acute kidney injury, epidemiology · Acute renal failure · Intensive care unit · Renal replacement therapy · Sepsis

Abstract

The epidemiology of acute kidney injury (AKI) has been difficult to explore in the past, due to different definitions across various studies. Nevertheless, this is a very important topic today in light of the high morbidity and mortality of critically ill patients presenting renal dysfunction during their stay in the intensive care unit (ICU). The case mix has changed over the years, and AKI is a common problem in critically ill patients often requiring renal replacement therapy (RRT). The RIFLE and AKIN initiatives have provided a unifying definition for AKI, making possible large retrospective studies in different countries. The present study aims at vali-

dating a unified web-based data collection and data management tool based on the most recent AKI definition/classification system. The interactive database is designed to elucidate the epidemiology of AKI in a critically ill population. As a test, we performed a prospective observational multicenter study designed to prospectively evaluate all incident admissions in ten ICUs in Italy and the relevant epidemiology of AKI. Thus, a simple user-friendly web-based data collection tool was created with the scope to serve for this study and to facilitate future multicenter collaborative efforts. We enrolled 601 consecutive incident patients into the study; 25 patients with end-stage renal disease were excluded, leaving 576 patients for analysis. The median age was 66 (IQR 53–76) years, 59.4% were male, while median Simplified Acute Physiology Score II and Acute Physiology and Chronic Health Evaluation II scores were 43 (IQR 35–54) and 18 (IQR 13–24), respectively. The most common diagnostic catego-

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ries for ICU admission were: respiratory (27.4%), followed by neurologic (17%), trauma (14.4%), and cardiovascular (12.1%). Crude ICU and hospital mortality were 21.7% and median ICU length of stay was 5 (IQR 3–14) days. Of 576 patients, 246 patients (42.7%) had AKI within 24 h of ICU admission, while 133 developed new AKI later during their ICU stay. RIFLE-initial class was Risk in 205 patients (54.1%), Injury in 99 (26.1%) and Failure in 75 (19.8%). Progression of AKI to a worse RIFLE class was seen in 114 patients (30.8% of AKI patients). AKI patients were older, with higher frequency of common risk factors. 116 AKI patients (30.6%) fulfilled criteria for sepsis during their ICU stay, compared to 33 (16.7%) of non-AKI patients ($p < 0.001$). 48 patients (8.3%) were treated with RRT in the ICU. Patients were started on RRT a median of 2 (IQR 0–6) days after ICU admission. AKI patients were started on RRT a median of 1 (IQR 0–4) day after fulfilling criteria for AKI. Median duration of RRT was 5 (IQR 2–10) days. AKI patients had a higher crude ICU mortality (28.8 vs. 8.1%, non-AKI; $p < 0.001$) and longer ICU length of stay (median 7 vs. 3 days, non-AKI; $p < 0.001$). Crude ICU mortality and ICU length of stay increased with greater severity of AKI. 225 (59.4% of AKI patients) had complete recovery of renal function, with a serum creatinine at time of ICU discharge which was $\leq 120\%$ of baseline; an additional 51 AKI patients (13.5%) had partial renal recovery, while 103 (27.2%) had not recovered renal function at the time of death or ICU discharge. The study supports the use of RIFLE as an optimal classification system to stage AKI severity. AKI is indeed a deadly complication for ICU patients, where the level of severity is correlated with mortality and length of stay. The tool developed for data collection was user-friendly and easy to implement. Some of its features, including a RIFLE class alert system, may help the treating physician to systematically collect AKI data in the ICU and possibly may guide specific decisions on the institution of RRT.

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Introduction

The epidemiology of acute kidney injury (AKI) has been difficult to explore in the past due to different definitions across various studies. Nevertheless, this is a very important topic today in light of the high morbidity and mortality of critically ill patients presenting renal dysfunction during their stay in the intensive care unit (ICU) [1]. The case mix has changed over the years, and AKI is a common problem in critically ill patients often requiring renal replacement therapy (RRT). The RIFLE and AKIN initiatives have provided a unifying definition for

AKI, making possible large retrospective studies in different countries [2–5]. RIFLE/AKIN define and stage AKI using serum creatinine (SCr), urine output (UO) and need for RRT, making them simple to apply in a variety of clinical and research settings [3]. The use of such definitions in the literature has increased gradually over the last 6 years [4–11]. The present study aims at validating a unified web-based data collection and data management tool based on the most recent AKI definition/classification system. A simple user-friendly web-based data collection tool was created with the scope to serve for this study and to facilitate future multicenter collaborative efforts. The interactive database is designed to elucidate the epidemiology of AKI in a critically ill population. As a test, we performed a prospective observational multicenter study designed to prospectively evaluate all incident admissions in ten ICUs in Italy and the relevant epidemiology of AKI. Our objectives were to determine the incidence of AKI among critically ill patients using consensus definitions, to characterize etiology and timing of AKI, and to evaluate clinical outcomes associated with AKI.

Methods

Creation of Database and Test Application

Although the evolution of numerous tools and methods has greatly improved over the years, the process of collecting accurate data can still be difficult; this is particularly true in situations where there are multiple study sites or offsite data collection is involved. The achievement of a well-established methodology of ten results from a multiple steps process that involves multidisciplinary fields like medical, engineering and statistical. Hence, in order to create a user-friendly data collection system, applicable in several ICUs, we undertook three subsequent development steps.

The archaic version of the electronic case report form was developed, as an Excel file, to evaluate the quality of the contribution of every field to the statistical analysis and the major error committed filling in the data (accuracy and compliance). A second system based on HTML and MS Access database permitted to eliminate the previous critical issues and to increment the cooperation of different centers allowing multiple simultaneous access from different locations; an evaluation of time spent to manage the information required was moreover estimated to improve next version. 300 patients in this step were enrolled as a pilot study. The third final and current generation of the program was based on the latest open source framework functionality. As a test of this latest version, a prospective observational study was done on adult patients (age ≥ 18 years) admitted to ten ICUs in Italy from September 2009 to April 2010 (participating centers are listed at the end of the article). The study protocol was reviewed by the ethics committees or institutional review boards of the participating centers. Because of the anonymous and noninterventional nature of the study, the ethics committees of study centers waived the need for informed consent.

AKI was defined using both the creatinine and UO criteria of the RIFLE classification [1]. A patient was considered to have AKI when he had an increase in SCr of at least 50% from baseline, or a reduction in UO to <0.5 ml/kg/h for more than 6 h (i.e. fulfilling at least class Risk). Clinical charts were reviewed for previous SCr values. Baseline renal function was defined as the lowest known SCr value during the preceding 3 months. For patients without known prior SCr, the baseline SCr was estimated by solving the MDRD equation, assuming a glomerular filtration rate of 75 ml/min/1.73 m², as recommended by the ADQI Working Group [1] and previously applied [10, 12]. Patients were classified daily using the RIFLE criteria. RIFLE-initial refers to their RIFLE class on the first day of AKI. RIFLE-max refers to the worst RIFLE class reached by a patient during his ICU stay. Patients were considered as having new AKI if they did not have AKI on ICU admission, but subsequently reached at least class Risk during their follow-up. AKI patients were considered as having worsening AKI if they later reached a higher RIFLE-max class compared to RIFLE-initial (i.e. Risk to Injury or Failure, or Injury to Failure) at any time during their ICU stay. Patients with RIFLE-initial class of Failure were considered as having worsening AKI if they later required RRT. RRT was initiated and conducted at the discretion of the responsible physicians. There were no standardized criteria to start or end RRT. For AKI patients, renal outcome at ICU discharge or death was defined as follows: complete recovery if discharge SCr was within 120% of baseline; partial recovery if discharge SCr was 121–150% of baseline, and non-recovery if discharge SCr was >150% of baseline or still receiving RRT.

Sepsis and systemic inflammatory response syndrome were diagnosed according to the definitions of the American College of Chest Physicians/Society of Critical Care Medicine [13]. Patients who fulfilled these criteria during their ICU admission were classified accordingly. The individual data elements for the Acute Physiology and Chronic Health Evaluation (APACHE) II score [14], Sequential Organ Failure Assessment (SOFA) score [15] and Simplified Acute Physiology Score (SAPS) II [16] were recorded on the day of ICU admission, and scores were automatically calculated. SOFA score was calculated daily.

Data Collection

Data from enrolled patients were entered into electronic case report forms resident on a password-protected web application. Centers could only have access to data relevant to their patients. Multiple data elements were collected for each patient. After usability test, a web-based system was designed based on an open source framework Ruby on Rails. Data were collected into a Mysql database. A web-based system was chosen to offer investigators the convenience of collecting and entering information from various locations within their own centers in a rapid, efficient and accurate manner. The web further offers the advantages of both centralization of information and coordination of multiple clinical trial processes. An automatic data verification system for each data field screens for missing or out of range values and data inconsistencies, and generates a visual user alert. The user is informed about the error and is asked to correct it in real time. The web tool is organized in eight distinct sections, with easy navigability from one section to another: (1) Demographics, anthropometrics, and admission diagnoses; (2) Comorbidities; (3) First ICU day; (4) Daily vital signs and laboratory values; (5) AKI; (6) RRT; (7) Sepsis, and (8) Outcomes/Case closure. In the 'Comorbidities' section, a his-

tory of exposure to nonsteroidal anti-inflammatory drugs, angiotensin-converting enzyme inhibitors (ACE-I), angiotensin-2-receptor blockers (ARB), aminoglycosides or radiocontrast prior to ICU admission was also recorded. Data from the 'First ICU day' section are used to automatically calculate APACHE II, SAPS II and SOFA scores. In the 'Daily vital signs and laboratory values' section, the 24-hour UO, the worst 12-hour UO, the worst 6-hour UO, and the worst SCr for that day are entered. The system then automatically displays the following items: the ratio of the day's SCr to the baseline SCr, the ratio of the day's SCr to the SCr within the previous 48-hour window, and the UO expressed as ml/kg/h. These aid the investigator in selecting the appropriate RIFLE and AKIN stage in the 'AKI' section. An optional alert can be activated when the patient reaches at least RIFLE class Risk. Use of diuretics was also recorded. In the 'AKI' section, the suspected factors contributing to AKI are entered. The 'RRT' section records indication for RRT, details of RRT prescription and delivery. In the 'Sepsis' section, the microorganism(s) and suspected source of infection are recorded. For 'Outcome', all-cause ICU and hospital (when available) mortality are entered. Periodic audits were performed to establish the accuracy of data capture and transfer into the database. An e-mail and/or telephone contact was made to the participating investigators requesting completion, correction, or verification of specific data items. Edit messages are retained in the file indicating the questionable data and any changes made when the requested information is returned. The final data were then imported into a statistical program for analysis.

Continuous variables are expressed as mean $\pm$ standard deviation or median (interquartile range) and compared between any two groups using t test or the Mann-Whitney U test, and among three groups using analysis of variance (general linear models with adjustment for multiple comparisons), as appropriate. Categorical variables are expressed as proportions and compared with the Mantel-Haenszel χ^2 test or Fisher exact test. Data were analyzed using the SPSS 14.0 (SPSS, Inc., Chicago, Ill., USA) software package, with two-sided p value <0.05 considered as statistically significant.

At the end of the study, a cross-check with the study participants and the internal review committee was done in order to establish a final evaluation of the data collection tool. The interface was evaluated in terms of user friendliness; the access to data input and data retrieval was discussed, and the easy transfer to a statistical program was also evaluated. A final general conclusion on scalability and applicability in future studies was then drawn from the obtained evaluations and results.

Data Collection Tool and Database Evaluation Results

The final version of the database collection tool has been defined by the users as easy to implement in the clinical routine. This indeed may become an important tool to collect patient's information, build statistics and generate epidemiology trials.

In figure 1, a screenshot of the patient management system is depicted. Figure 2 describes a step for a 'new

ID Code	Race	Birthdate	H	W	Admission	ICU	ICU type	Diagnosis ICU
075H200829508	White	25 January 1955	168	70.0	18 November 2008	20 November 2008	Respiratoire	ALI (Acute Lung Injury)
09R0200839901	White	17/07/1942	165	65.0	20/11/2008	20/11/2008	Neurologie	Aneurisma/RAV con sanguinamento
028M200840087	White	23/12/1947	165	85.0	21/11/2008	21/11/2008	Neurologie	Sanguinamento intracranico
13AA200840128	White	26/04/1924	180	88.0	22/11/2008	22/11/2008	Trauma	Polltrauma
03MM200839765	White	18/09/1936	160	70.0	19/11/2008	22/11/2008	Respiratoire	ARDS
14GD200840177	White	20/12/1976	179	80.0	23/11/2008	24/11/2008	Trauma	Polltrauma
07CG200840191	White	12/04/1966	182	85.0	24/11/2008	24/11/2008	Trauma	Polltrauma
13HG200840386	White	12/10/1940	165	65.0	25/11/2008	25/11/2008	Neurologie	Sanguinamento intracranico
01CF200840608	White	26/02/1936	178	90.0	27/11/2008	27/11/2008	Trauma	Trauma toracico

Fig. 1. Patient management. A screen shot of the first page of the NEFROINT system. The list of the patients recorded displays the most important information to be inserted. Edit and Delete fields are available on the right. With the Show button, one may enter the specific Patient CRF.

patient' creation. At any time, review of data recorded is possible as shown in figures 3 and 4. The MDRD calculation of GFR is useful to estimate baseline creatinine and to help with RIFLE class definition.

In figures 5 and 6, the most important laboratory data are displayed together with the fields required to calculate APACHE II, SAPS II and SOFA scores. New Lab records can be created with a simple but effective automatic data verification system (fig. 7, 8). An interesting feature of the program is the RIFLE alert alarm. When a patient reaches a given class of AKI, a pop-up alarm blinks, and the operator may decide for a RIFLE-based application of a RRT technique (fig. 9, 10). The database contains a section dedicated to continuous RRT (CRRT) (fig. 11) and a verification tool (fig. 12) to assess possible errors in data entry.

Demographics and AKI Epidemiology Results

We enrolled 601 consecutive incident patients into the study; we excluded 25 patients with end-stage renal disease on chronic RRT, leaving 576 patients for analysis.

Patient characteristics are shown in table 1. The median age was 66 (IQR 53–76) years, 59.4% were male, while median SAPS II and APACHE II scores were 43 (IQR 35–54) and 18 (IQR 13–24), respectively. The most common diagnostic categories for ICU admission were: respiratory (27.4%), followed by neurologic (17%), trauma (14.4%), and cardiovascular (12.1%). SCr values prior to hospitalization were available for only 45.8% of patients; for the rest, the baseline SCr was estimated using MDRD. The proportion of patients in which the MDRD estimation was used was similar among AKI and non-AKI patients. The median baseline premorbid SCr was 1.0 (IQR 0.8–1.1) mg/dl. Crude ICU and hospital mortality were 21.7%, and median ICU length of stay was 5 (IQR 3–14) days.

Of 576 patients, 246 (42.7%) had AKI within 24 h of ICU admission, while 133 developed new AKI later during their ICU stay (fig. 13). The most commonly reported factors contributing to AKI were hypovolemia (29.5%), septic shock (13.5%), major surgery (12.1%) and cardiogenic shock (11.8%). RIFLE-initial class was Risk in 205 patients (54.1%), Injury in 99 (26.1%) and Failure in 75 (19.8%). Progression of AKI to a worse RIFLE class was seen in 114 patients (30.8% of AKI patients).

Clinic Cases Management

Show: opened, closed, all. Search:

ID-Code	Race	BirthDay	H	W	Admission	ICU	ICU type	Diagnosis ICU
---------	------	----------	---	---	-----------	-----	----------	---------------

Create Clinic Case

*ID (Cf) - Identification:

*Race:

*Sex:

*Birthdate:

*Height: [cm]

*Weight:

Hospital Admission:

*Date:

*Hospital Admission:

Diagnosis:

ICU Admission:

*Date:

*ICU Admission:

ICU Diagnosis:

Score and other informations

*Patient Type:

*Chronic Diseases:

Fig. 2. Create new patient fields. Here, general patient information is collected to permit the identification of the patient type, the reason and the date of admission to hospital and ICU.

Main | Log in | Clinic cases | Data | Administration | About

Nefroint

Currently logged on as: francesco, Logout

Case review: 05ZG200841268

Entered ICU on 2008-12-02 and was closed on 2008-12-29

SOFA	9
SCORES (read)	SAPS II 44 Predicted Death Rate = 33%
APACHE II	19 Predicted Death Rate = 32%
SEPSI	N/A
Last IRA date	2008-12-29
IRA sessions	28 sessions recorded on 28 days
Last Lab date	2008-12-29
Lab duration	28 sessions recorded on 28 days
Last RRT date	N/A
RRT duration	0 days

Temperature=1 MAP=2 Heart Rate=0 Respiratory Rate=0
 FiO2-(A-a)O2=1 pH=3 Na=0 K=0 Creatinine(1.06/1.0=>No ARF)=0 HCT=0
 WBC=1 GCS=0 Age=6 Chronic Organ Insufficiency=5
 Predicted Death Rate = 32%

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 Laboratory
 IRA
 RRT
 Sepsis
 Case closure

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Fig. 3. Review page is useful to monitor the progress of the data recorded. The amount of days recorded and the last date for every section are reported. SOFA, SAPS II and APACHE II are automatically calculated from the 'First ICU day' section. Pop-up window reports the score details.

Main Log in Clinic cases Administration About

Nefroint Currently logged on as: francesco, Logout

Case Details of erg

☐ Creat. Pre ☐ Known/Estimate
 mg/dl ☐ Known ☐ Estimate from MDRD

Clinic case Pathologies:

Urinary
 Hypertension

Farmac Nefrotossici:

☐ Fans ☐ Aminoglycosides ☐ Acei/Antag.rec.AT1 ☐ O

Create Cancel

Age (years)	Black Males (mg/dL mcmmol/L)	White Males (mg/dL mcmmol/L)	Black Females (mg/dL mcmmol/L)	White Females (mg/dL mcmmol/L)
20-24	1.5 133	1.3 115	1.2 106	1.0 88
25-29	1.5 133	1.2 106	1.1 97	1.0 88
30-39	1.4 124	1.2 106	1.1 97	0.9 80
40-54	1.3 115	1.1 97	1.0 88	0.9 80
55-65	1.3 115	1.1 97	1.0 88	0.8 71
>65	1.2 106	1.0 88	0.9 80	0.8 71

Estimated GFR = $75 \text{ (ml/min/1.73m}^2\text{)} = 186 \times (\text{SCr})^{-1.154} \times (\text{Age})^{-0.203} \times (0.742 \text{ if female}) \times (1.210 \text{ if African-American}) = \exp(5.228 - 1.154 \times \ln(\text{SCr}) - 0.203 \times \ln(\text{Age}) - (0.299 \text{ if female}) + (0.192 \text{ if African-American}))$

Recommendation: When baseline creatinine is unknown, it should be estimated from the MDRD equation.

Fig. 4. Case Detail section. The figure shows the pop-up image that helps in MDRD estimation.

Scores for 123

HR H SBP H MAP H T pH pCO2 pO2 HCO3 FiO2 WBC H hct Na K Urea Creat GCS Urin

Create Score

*Heart rate Lowest [bpm] *Heart rate Highest [bpm] *SBP lowest [mmHg] *SBP highest [mmHg] *MAP lowest [mmHg] *MAP Highest [mmHg] *Temp Lowest [°C] *Temp Highest [°C]

Hemogas

*pH *pCO2 [mmHg] *pO2 [mmHg] *HCO3 [mmol/L] *FiO2 [%] *PaO2/FiO2

Hemocrome

*WBC Lowest [x10⁹/L] *WBC Highest [x10⁹/L] *Hct [%] *Platelet

Chemical

*Na [mEq/l] *K [mEq/l] *Urea [mg/dl] *Creatinine [mg/dl] *Bilirubin [mg/dl]

Other Informations

*Breath rate highest [bpm] *Urine output [ml] *Urine out. H [h] *GCS *Ventilation *Sofa Cardiovascular

Create Cancel

APACHE II

SAPS II

SOFA

Fig. 5. First ICU day. Only 29 fields are required to calculate SOFA, SAPS II and APACHE II. Single score calculation would require the compilation of 39 fields: SOFA 8 fields, SAPS II 15 fields, APACHE II 16 fields; 39 in total.

nefroint.nephro.it/lab_records/list

ick access, place your bookmarks here on the bookmarks bar. [Import bookmarks now...](#)

Main Log in Clinic cases Data Administration About

Nefroint

Warning: the selected case is closed

Currently logged on as: francesco, Logout

Lab Records for 052G200841268

Date	Urine 24h	Urine 12h	Urine 6h	Creat.	Net Fluid	Urea	GCS	Ventilation	Diuretic	
03/12/2008	2320	1070	370	0.91	905	79	15	4	false	Edit Delete
04/12/2008	1760	960	430	0.73	4101	72	15	4	true	Edit Delete
05/12/2008	5120	2100	800	0.82	-500	70	15	4	true	Edit Delete
06/12/2008	4150	2000	1000	0.87	1320	80	15	4	true	Edit Delete
07/12/2008	4100	1700	600	0.83	-500	78	15	4	true	Edit Delete
08/12/2008	3800	1850	750	0.87	-1070	92	15	4	false	Edit Delete
09/12/2008	3530	1730	630	0.83	-100	80	15	4	false	Edit Delete
10/12/2008	3150	1400	600	0.74	-24	61	15	4	false	Edit Delete
11/12/2008	2620	1270	550	0.62	820	54	15	4	false	Edit Delete
12/12/2008	1920	950	350	0.68	1578	58	15	4	true	Edit Delete
13/12/2008	1860	790	350	0.57	1040	53	15	4	false	Edit Delete
14/12/2008	1560	710	300	0.61	1720	64	15	4	true	Edit Delete
15/12/2008	3900	1450	500	0.65	-680	60	15	4	true	Edit Delete
16/12/2008	3450	1300	550	0.77	250	60	15	4	true	Edit Delete
17/12/2008	5100	2250	850	0.77	-2512	54	15	4	true	Edit Delete
18/12/2008	4000	1900	800	0.77	-875	58	15	4	true	Edit Delete
19/12/2008	6450	1875	675	0.76	-3214	61	15	4	false	Edit Delete
20/12/2008	7760	3350	800	0.60	60	60	15	4	false	Edit Delete

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Fig. 6. The most important laboratory data are listed when the section is opened. Ascending and descending order is provided for date, UO, creatinine, net fluid balance, urea, etc. Edit and Delete functions on records are always available.

Create Lab Record

Date [ml] [ml] [ml] [ml]

*Urine 24 Hour *Urine worst 12h *Urine worst 6h *Net Fluid Balance

*Urea [mg/dl] *Creatinine [mg/dl] K [mEq/l] Albumin [g/dl] Bilirubin [mg/dl] Lowest glucose [mg/dl] Highest glucose [mg/dl]

*PLT [x10⁹] Hemoglobin [g/dl] WBC [x10⁶/ml]

Other informations

*Diuretic use ☐ Yes ☐ No *Ventilation *PaO₂/FiO₂ [mmHg] pH HCO₃ [mmol/L] *GCS *Sofa Cardiovascular

Create Cancel

Fig. 7. The screen shot of 'Create Lab Record' displays twelve compulsory fields marked with an asterisk, as well as nine optional fields. Daily SOFA score is estimated by the 'Other informations' section.

“LABORATORY” SECTION

Man, caucasic, 70Kg, Urin Output 6 h = 190 ml

$190 < 0.5 \times 70 \times 6 = 210 \Rightarrow$ Urin Output 12h is request for RIFLE class “I”

Fig. 8. Automatic data verification system for conditioned data. The displayed case requires 12-hour UO to evaluate RIFLE I class.

Fig. 9. A simple RIFLE alert can be activated to help in medical decision without any supplementary operation. Early start of CRRT may depend on this pop-up RIFLE class alarm.

Ira Records for erg

Create Ira Record

Ira date: 25 June 2008

Update Ira Record

Lab report creatinine:

2009-01-07 = 0.44 [mg/dl] (Today)

2009-01-06 = 0.36 [mg/dl]

2009-01-05 = 0.33 [mg/dl]

Case Details report Creatinine Pre at: 0.7 [mg/dl] ; Today/Pre = 0.44/0.7 = 0.6

Urin Output Criteria:

Dis 6 H = 650 [ml] and 0.5*weight*6h = 210 [ml]

Dis 12 H = 2000 [ml] and 0.5*weight*12h = 420 [ml]

Dis 24 H = 4810 [ml] and 0.3*weight*24h = 504 [ml]

Ira date: 7 January 2009

*RIFLE: E

*AKIN: ESKD

RRT: Major ira reason: Other

Minor reason 1:

Minor reason 2:

GFR Criteria*

Urine Output Criteria

Risk: Increased creatinine x1.5 or GFR decrease > 25%

Injury: Increased creatinine x2 or GFR decrease > 50%

Failure: Increase creatinine x3 or GFR dec > 75% or creatinine ≥ 4mg/dl (Acute rise of > 0.5 mg/dl)

Loss: Persistent ARF** – complete loss of renal function > 4 weeks

ESRD: End Stage Renal Disease

High Sensitivity

High Specificity

Oliguria

UO < .5ml/kg/h x 6 hr

UO < .5ml/kg/h x 12 hr

UO < .3ml/kg/h x 24 hr or Anuria x 12 hrs

Fig. 10. RIFLE and AKIN criteria are supported by the corresponding decision schema. An important tool reports the ratio of the day's SCr to the baseline SCr, the ratio of the day's SCr to the SCr within the previous 48-hour window, and the UO expressed as ml/kg/h. The criteria are estimated without any type of calculation.

Rrt Records for 12BMJ

Create Rrt Record

Rrt date: 15 December 2008

RRT Modality: [dropdown]

Blood flow (Qb): [input] [ml/min]

*Net fluid remov.: [input] [ml/H]

*Prescribed duration: [input] [h]

*Actual duration: [input] [h]

Anticoagulants: [dropdown]

Terminated Today: [checkbox]

Initial Reasons of CRRT - Vascular access informations [show](#)

Primary: [dropdown]

Secondary: [dropdown]

Tertiary: [dropdown]

Vascular access site: [dropdown]

Vascular access side: [dropdown]

Create **Cancel**

Fig. 11. The section is totally dedicated to CRRT treatment. Indication for RRT, details of RRT prescription and delivery are recorded here.

Lab Records for tre Create New

Date Urine 24h Urine 12h Urine 6h Creat. Net Fluid Urea GCS Ventilation Diuretic

Create Lab Record

10 errors prohibited this lab record from being saved

There were problems with the following fields:

- Urine 24h out of range [1-15000] ml
- Urine 24h Unit of measure is [ml]. Only Integer
- Urea out of range [1-500] mg/dl
- Plt out of range [1-999]x1000/μl
- Diuretic use Select diuretic Yes or No
- Net fluid balance out of range [-10000 to 10000] ml
- Net fluid balance Only integer. Unit of measure is [ml]
- Creatinine out of range [0.5-20] mg/dL
- Ventilation can't be blank
- Urine worst 12h is required when urine 6h < 0.5*weight*6

Date *Urine 24 Hour Urine worst 12h *Urine worst 6h *Net Fluid Balance

25 September 2008 [ml] [ml] 122 [ml] [ml]

*Urea *Creatinine Albumin Bilirubin Lowest glucose Highest glucose

[mg/dl] [mg/dl] [g/dl] [mg/dl] [mg/dl] [mg/dl]

*PLT Hemoglobin WBC

[x10⁹] [g/dl] [x10⁶/ml]

Other informations

*Diuretic use *Ventilation *PaO₂/FiO₂ *GCS *Sofa Cardiovascular

☐ Yes ☐ No [mmHg] [mmHg] [mmHg]

Create **Cancel**

23/09/2008	1212	-	1211	12.0	123	12	12	No	false	Edit Delete
24/09/2008	12	-	400	12.0	123	12	12	Invasive	false	Edit Delete

Fig. 12. Each section contains specific data verification tool. Missing, out of range, obligatory and 'conditioned' fields as well as inconsistencies in data are verified before the validation and registration of the section.

Among these patients, it took a median of 2 (IQR 1–6) days to attain their maximum RIFLE class. RIFLE-max was Risk in 127 patients (33.5%), Injury in 130 (34.3%) and Failure in 122 (32.2%).

AKI patients were older, more likely to be male, and have a history of cardiovascular disease and hypertension, and to have had exposure to ACE-I or ARBs prior to their hospitalization. They were more likely to have a respiratory or trauma diagnosis on ICU admission, and had higher APACHE II, SAPS II, and SOFA scores. On their first ICU day, AKI patients were more likely to be on vasopressors, but the proportion of patients on mechanical ventilation was similar between the two groups. AKI patients also had lower mean arterial pressure, UO, pH, pO₂ and PaO₂/FiO₂ values, and higher urea and SCr values on ICU admission. 116 AKI patients (30.6%) fulfilled criteria for sepsis during their ICU stay, compared to 33 (16.7%) of non-AKI patients ($p < 0.001$).

48 patients (8.3%) were treated with RRT in the ICU; 2/48 did not fulfill criteria for AKI and received RRT for nonrenal indications. Overall, patients were started on RRT a median of 2 (IQR 0–6) days after ICU admission. AKI patients were started on RRT a median of 1 (IQR 0–4) day after fulfilling criteria for AKI. Median duration of RRT was 5 (IQR 2–10) days.

AKI patients had a higher crude ICU mortality (28.8 vs. 8.1%, non-AKI; $p < 0.001$) and longer ICU length of stay (median 7 vs. 3 days, non-AKI; $p < 0.001$) (fig. 4). Crude ICU mortality and ICU length of stay increased with greater severity of AKI. 225 patients (59.4% of AKI patients) had complete recovery of renal function, with an SCr at time of ICU discharge which was $\leq 120\%$ of baseline; an additional 51 AKI patients (13.5%) had partial renal recovery, while 103 (27.2%) had not recovered renal function at the time of death or ICU discharge.

Fig. 13. Epidemiology of AKI derived from the NEFROINT database. The asterisk signifies at ICU discharge or death.

Sepsis events were recorded throughout patient's stay in the ICU; 149 patients (25.9%) fulfilled criteria for sepsis. Of these, 116/149 (77.8%) had AKI, compared to 263/427 (61.6%) nonseptic patients ($p < 0.001$). Septic AKI patients tended to fulfill criteria for both sepsis and AKI on the same day; in a few cases, sepsis preceded AKI (median days from sepsis criteria to AKI criteria, 0, IQR 0–1). Septic patients had more severe AKI, and were more likely to receive RRT, had higher ICU mortality and longer ICU stay in agreement with international database results [11].

Discussion

This is the first Italian multicenter prospective data collection to establish the epidemiology of AKI in the ICU. The study confirms previous analyses describing

RIFLE as an optimal classification system to stage AKI severity. AKI is indeed a deadly complication for ICU patients where the level of severity correlated with mortality and length of stay. The tool developed for data collection was user friendly and easy to implement. Some of its features, including a RIFLE class alert system, may help the treating physician to collect systematically AKI data in the ICU and may possibly guide specific decision on the institution of RRT. Developing a user-friendly interface has been demanding and time-consuming. The approach was consistent with the current view that database entry methodology should be simple and easy to correct and control. Physicians and nurses in the ICU have very little time to comply with complicated studies requiring time-consuming procedures for data input. The current version of the NEFROINT database seems to respond to the requirements of simplicity together with internal accurate and sophisticated management of data. We feel

Table 1. Characteristics of the cohort by presence or absence of AKI

	All	AKI	Non-AKI	p
Patients	576	379	197	
Males	352 (59.4)	237 (62.5)	105 (53.3)	0.039
Age, years	66 (53–76)	69 (58–78)	59 (43–72)	<0.001
Body weight, kg	75 (65–80)	75 (65–85)	70 (60–80)	<0.001
Height, cm	170 (160–175)	170 (160–175)	170 (162–175)	0.274
Hypertension	270 (46.9)	198 (52.2)	72 (36.5)	0.001
Diabetes	108 (18.7)	79 (20.8)	29 (14.7)	0.2
Cardiovascular disease	249 (43.2)	183 (48.3)	66 (33.5)	0.003
History of chronic kidney disease	36 (6.2)	26 (6.9)	10 (5.1)	0.471
History of proteinuria or hematuria	12 (2.1)	11 (2.9)	1 (0.5)	0.067
Baseline creatinine, mg/dl	1.0 (0.8–1.1)	1.0 (0.8–1.1)	1.0 (0.8–1.2)	0.457
Medications				
NSAID	56 (9.7)	38 (10.0)	18 (9.1)	0.769
ACE-I or ARB	95 (16.5)	71 (18.7)	24 (12.2)	0.045
Patient type				
Medical	273 (47.4)	194 (51.2)	79 (40.1)	0.014
Elective surgery	117 (20.3)	73 (19.3)	44 (22.3)	0.385
Emergency surgery	186 (32.3)	112 (29.5)	74 (37.6)	0.06
Admission diagnosis				
Respiratory	158 (27.4)	115 (30.3)	43 (21.8)	0.031
Neurologic	98 (17.0)	50 (13.2)	48 (24.4)	0.001
Trauma	83 (14.4)	44 (11.6)	39 (19.8)	0.012
Cardiovascular	70 (12.1)	60 (15.8)	10 (5.1)	<0.001
Gastrointestinal	32 (5.6)	22 (5.8)	10 (5.1)	0.849
ICU admission				
SOFA	5 (3–7)	6 (4–8)	4 (3–6)	<0.001
SAPS II	43 (35–54)	44 (37–55)	42 (32–53)	0.0023
APACHE II	18 (13–24)	19 (14–25)	17 (12–21)	<0.001
Creatinine, mg/dl	0.9 (0.7–1.4)	1.1 (0.8–1.6)	0.8 (0.6–1.0)	<0.001
Urea, mg/dl	41 (27–64)	50 (32–78)	33 (22–44)	<0.001
Urine output first ICU day, ml	925 (500–1,635)	800 (450–1,380)	1,250 (750–1,950)	<0.001
Na, mEq/l	140 (137–143)	140 (137–144)	139 (137–142)	0.0232
K, mEq/l	3.8 (3.5–4.2)	3.9 (3.6–4.4)	3.7 (3.5–4.0)	<0.001
Bilirubin, mg/dl	0.7 (0.5–1.1)	0.7 (0.5–1.0)	0.7 (0.5–1.2)	0.672
Hematocrit, %	32 (28–36)	32 (28–36)	32 (28–35)	0.913
WBC (× 1,000)	11 (8–16)	11 (8–16)	10 (8–15)	0.515
Platelets	188 (127–250)	184 (124–248)	191 (138–253)	0.383
pH	7.40 (7.33–7.45)	7.39 (7.32–7.45)	7.40 (7.36–7.47)	<0.001
pCO ₂ , mm Hg	38 (33–45)	38 (33–45)	38 (32–43)	0.072
pO ₂ , mm Hg	114 (82–156)	110 (79–150)	122 (88–161)	0.026
HCO ₃ , mEq/l	23 (21–26)	23 (20–26)	23 (21–26)	0.30
PaO ₂ /FiO ₂	253 (161–366)	230 (156–342)	286 (189–420)	<0.001
Mechanical ventilation, %	532 (92.4)	353 (93.1)	179 (90.9)	0.326
Use of vasopressors, %	148 (25.7)	115 (30.4)	33 (16.8)	<0.001
Dopamine/dobutamine ≤5 µg/kg/min	45 (7.8)	37 (9.8)	8 (4.1)	0.014
Dopamine/dobutamine ≤5 or epinephrine/norepinephrine ≤0.1 µg/kg/min	45 (7.8)	31 (8.2)	14 (7.1)	0.744
Epinephrine/norepinephrine >0.1 µg/kg/min	58 (10.1)	47 (12.4)	11 (5.6)	0.009
Sepsis	149 (25.9)	116 (30.6)	33 (16.7)	<0.001
Outcome				
ICU mortality	125 (21.7)	109 (28.8)	16 (8.1)	<0.001
ICU length of stay, days	5 (3–14)	7 (3–16)	3 (2–8)	<0.001

Figures in parentheses indicate percentage or range.

that this approach may represent a potential pathway towards large multicenter studies to be undertaken in the near future.

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References

- 1 Bellomo R, et al: 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* 2004; 8:R204–R212.
- 2 Mehta RL, et al: Acute Kidney Injury Network: report of an initiative to improve outcomes in acute kidney injury. *Crit Care* 2007; 11:R31.
- 3 Cruz DN, Ricci Z, Ronco C: Clinical review: RIFLE and AKIN – time for reappraisal. *Crit Care* 2009;13:211.
- 4 Ricci Z, Cruz D, Ronco C: The RIFLE criteria and mortality in acute kidney injury: a systematic review. *Kidney Int* 2008;73:538–546.
- 5 Ostermann M, Chang RW: Acute kidney injury in the intensive care unit according to RIFLE. *Crit Care Med* 2007;35:1837–1843.
- 6 Bagshaw SM, et al: A multi-centre evaluation of the RIFLE criteria for early acute kidney injury in critically ill patients. *Nephrol Dial Transplant* 2008;23:1203–1210.
- 7 Thakar CV, et al: Incidence and outcomes of acute kidney injury in intensive care units: a Veterans Administration study. *Crit Care Med* 2009;37:2552–2558.
- 8 Cruz DN, et al: Diagnostic and staging criteria for acute kidney injury: do we need prospective studies? *Minerva Anestesiol* 2008; 74(suppl 1):303–305.
- 9 Fiaccadori E, et al: Predicting patient outcome from acute renal failure comparing three general severity of illness scoring systems. *Kidney Int* 2000;58:283–292.
- 10 Cruz DN, et al: North East Italian Prospective Hospital Renal Outcome Survey on Acute Kidney Injury (NEiPHROS-AKI): targeting the problem with the RIFLE Criteria. *Clin J Am Soc Nephrol* 2007;2:418–425.
- 11 Uchino S, et al: Acute renal failure in critically ill patients: a multinational, multicenter study. *JAMA* 2005;294:813–818.
- 12 Uchino S, et al: An assessment of the RIFLE criteria for acute renal failure in hospitalized patients. *Crit Care Med* 2006;34:1913–1917.
- 13 Levy MM, et al: 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. *Crit Care Med* 2003;31:1250–1256.
- 14 Knaus WA, et al: APACHE II: a severity of disease classification system. *Crit Care Med* 1985;13:818–829.
- 15 Vincent JL, et al: Use of the SOFA score to assess the incidence of organ dysfunction/failure in intensive care units: results of a multicenter, prospective study. Working group on 'sepsis-related problems' of the European Society of Intensive Care Medicine. *Crit Care Med* 1998;26:1793–1800.
- 16 Le Gall JR, Lemeshow S, Saulnier F: A new Simplified Acute Physiology Score (SAPS II) based on a European/North American multicenter study. *JAMA* 1993;270:2957–2963.