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Acute kidney injury in critically ill patients classified by AKIN versus RIFLE using the SAPS 3 database

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Abstract *Objective:* Acute kidney injury (AKI) is associated with significantly increased morbidity and mortality. To provide a uniformly accepted definition, the RIFLE classification was introduced by the Acute Dialysis Quality Initiative, recently modified by the Acute Kidney Injury Network (AKIN), suggesting staging of AKI based on dynamic changes within 48 h. This study compares these two classification systems with regard to outcome. *Design:* Cohort analysis of SAPS 3 database. *Measurements:* Sixteen thousand seven hundred and eighty-four ICU patients from 303 ICUs were analysed. Classification was performed according to RIFLE (Risk, Injury, Failure) or according to AKIN (stage 1, 2, 3) without including a requirement of renal replacement therapy in the analysis. Changes of serum creatinine as well as urinary output were assessed for both AKIN and RIFLE during the first 48 h of ICU admission. Primary endpoint was hospital mortality. *Results:* Incidence of AKI in our population of critically ill patients was found to range between 28.5 and 35.5% when applying AKIN and RIFLE criteria, respectively, associated with increased hospital mortality averaging 36.4%. Observed-to-expected mortality ratios revealed excess mortality conferred by any degree of AKI increasing from 0.81 for patients classified as non-AKI up to 1.31 and 1.23 with AKIN stage 3 or RIFLE Failure, respectively. AKIN misclassified 1,504 patients as non-AKI compared to RIFLE which misclassified 504 patients. *Conclusion:* Acute kidney injury classified by either RIFLE or AKIN is associated with increased hospital mortality. Despite presumed increased sensitivity by the AKIN classification, RIFLE shows better robustness and a higher detection rate of AKI during the first 48 h of ICU admission.

Keywords Acute kidney injury · Epidemiology · Incidence · Outcome · Urinary output · Creatinine

Introduction

Acute kidney injury (AKI) is associated with both significant morbidity and mortality [1–4]. This has clearly been demonstrated in critically ill patients requiring renal replacement therapy (RRT) following AKI where excessive mortality is observed after correction for age, gender and severity of disease [1]. Even a relatively modest impairment of renal function must be considered an independent risk factor for mortality [5]. The incidence of

AKI appears to be increasing [4], although exact numbers are difficult to quantify given the lack of a uniform definition of AKI with more than 30 definitions already published [6]. A step in the right direction was the development of the RIFLE criteria by the Acute Dialysis Quality Initiative (ADQI) [3] which utilizes changes in serum creatinine and urinary output (UO) as markers of renal dysfunction. On the basis of these two parameters, AKI is classified into Risk, Injury and Failure, with two additional classes LOSS and ESKD (=End-stage Kidney Disease) defined by the requirement of RRT for more than 4 weeks and more than 3 months, respectively [3]. Since its initial publication, several studies have investigated the validity of the RIFLE criteria to classify AKI in terms of both severity and outcome [7–10].

The RIFLE classification is considered to suffer from two shortcomings. Firstly, it relies on prior knowledge of the baseline creatinine and does not necessarily reflect acuity of renal functional impairment. Secondly, the influence of the requirement of RRT on RIFLE stages has not yet been clearly defined. Therefore, a modification of the RIFLE classification was introduced by the Acute Kidney Injury Network (AKIN) including three new aspects [11]. First, it introduces an increase in serum creatinine by ≥0.3 mg/dl for classification of AKI. Secondly, changes in serum creatinine are determined within a time window of 48 h instead of referring to a baseline value. Finally, the requirement of RRT is taken into consideration for staging. Similar to the RIFLE system, AKI is classified into stages 1–3, an indication for RRT automatically determining stage 3 [12]. First external evaluations of this classification system proposed by AKIN have been tried recently in three studies [13–15], one of them representing retrospectively a single centre analysis including only 662 patients [14], the second one applying only a 24-h observation period [13] and the third one not including the UO criterion [15].

The aim of this study was (1) to evaluate the occurrence of AKI within 48 h of ICU admission, (2) to compare the effect of classifying patients according to AKIN or RIFLE criteria on epidemiology and mortality and (3) to understand the relative contribution of the urine output and creatinine portions of these criteria using the large, prospectively collected multicenter international database of the SAPS 3 project. The preliminary results of the study were presented at the 20th annual Congress of ESICM [16].

Methods

SAPS 3 database

The SAPS 3 Hospital Outcome Cohort comprises 16,784 patients from 303 ICUs. Data were collected at ICU admission, on days 1 and 2 of the ICU stay. Data quality was excellent as presented in the SAPS 3 primary report [17] (detailed description in ESM).

Classification of acute kidney injury

After exclusion of patients with chronic renal failure as defined by the SAPS 3 handbook (i.e. chronic renal supportive therapy for irreversible renal disease or history of chronic renal insufficiency at a sufficient level to provoke visceral effects) or kidney transplantation, AKI was classified by systems: AKIN and RIFLE.

AKIN classification

The AKIN classification system was introduced by the Acute Kidney Injury Network (AKIN) [11] (Table 1).

Table 1 Definition and classification (staging) for acute kidney injury

	Serum creatinine criteria	Urinary output criteria
AKIN classification [11]		
Stage 1	≥0.3 mg/dl (26.2 μmol/l) or ≥150–200% increase from baseline serum creatinine	<0.5 ml/kg/h for ≥6 h
Stage 2	>200–299% increase from baseline serum creatinine	<0.5 ml/kg/h for ≥12 h
Stage 3	≥300% increase from baseline serum creatinine or absolute serum creatinine ≥4.0 mg/dl (354 μmol/l) with an acute rise ≥0.5 mg/dl (44 μmol/l) or initiation of RRT	<0.3 ml/kg/h for ≥24 h or anuria ≥12 h
RIFLE classification [3]		
Risk	≥1.5-fold increase from baseline serum creatinine or decrease in GFR ≥25%	<0.5 ml/kg/h for ≥6 h
Injury	≥2.0-fold increase from baseline serum creatinine or decrease in GFR ≥50%	<0.5 ml/kg/h for ≥12 h
Failure	≥3.0-fold increase from baseline serum creatinine or decrease in GFR ≥75% or absolute serum creatinine ≥4.0 mg/dl (354 μmol/l) with an acute rise ≥0.5 mg/dl (44 μmol/l)	<0.3 ml/kg/h for ≥24 h or anuria ≥12 h

The AKIN stage was calculated within the first 48 h of admission (day 0–day 2). Serum creatinine on ICU admission was used as reference, staging was based on any increase within the 48 h observation as required by the definition with at least two measurements being necessary. Declines in serum creatinine were not coded as AKI. For the UO criterion the lowest UO during the 48-h period was used for staging. Since the SAPS 3 database does not contain data on the proportion of patients receiving acute RRT, this criterion could not be evaluated in our study.

RIFLE classification

RIFLE criteria were designed by the ADQI in order to obtain a general definition of AKI [3] (Table 1).

RIFLE class was determined within the first 48 h of admission (day 0–day 2). Baseline serum creatinines were calculated by the simplified "modification of diet in renal disease" (MDRD) formula assuming a glomerular filtration rate (GFR) of 75 ml/min/1.73 m^2 for all patients [3].

Classification of urinary output

Since our database does not track UO at 6 h, but only for 24 h, one cannot distinguish between the subgroups of AKIN (stage 1 and 2) and RIFLE (Risk and Injury). Under the assumption that the requirement of the UO to be less than 0.5 mg/kg/h for 24 h is more stringent than for 6 h we assigned all patients with UO <0.5 ml/kg/h to AKIN stage 2 or RIFLE Injury.

Statistical analysis

Statistical analysis was performed using SAS software, version 9.1 (SAS Institute, Cary, NC, USA). Unless otherwise specified, descriptive results are expressed as median and first and third quartiles. Student's *t* test or Wilcoxon's rank-sum test if appropriate was used to compare quantitative variables between groups. The chi-square test was used for categorical variables. A *P* value of 0.05 (two-sided) was considered significant. Observed-to-expected (O/E) mortality ratios were calculated by dividing the number of observed deaths per group by the number of expected deaths per group (as predicted by the SAPS 3). To test for statistical significance, we calculated 95% confidence intervals (CI) according to the method described by Hosmer and Lemeshow [18].

Multiple logistic regressions were constructed to explore the influence of AKIN or RIFLE groups, respectively, on vital status at hospital discharge (hospital mortality) as the dependent variable additional to the corrected SAPS 3 score (calculated as original SAPS 3 score minus the allocated creatinine points).

Results

Starting from the SAPS 3 Hospital Outcome Cohort 14,356 patients from 300 ICUs were finally included for analysis (Fig. 1).

The patients in the cohort under analysis had a median age of 63 (49–74) years, and 39.2% were female. Approximately 40% of the patients did not undergo a surgical procedure and roughly 50% were admitted after elective or acute surgery. Overall hospital mortality was 21.7% (Table 2).

AKI defined by AKIN

Using the criteria of AKIN within the first 2 days of ICU admission, AKI occurred in 4,093 patients (28.5%) with 1,077 (7.4%) in stage 1, 1,003 (7.2%) in stage 2 and 1,983 (13.8%) in stage 3 (Fig. 1).

Five hundred and ninety-six patients (4.2%) assigned to stage 1 were classified exclusively on the basis of an increase in serum creatinine $\geq$0.3 mg/dl. Demographics for each AKIN class are presented in ESM (Table E1).

Excluding patients who stayed in the ICU less than 2 days did not change the distribution of AKI stages significantly. Hospital mortality was increased for all patients qualifying for stages 1–3. However, mortality of patients classified as stage 2 appeared to be slightly lower than those classified as stage 1 (Table 3), which was also reflected by the 30-day mortality of the respective stages (Fig. 2a).

When comparing mortalities expected by the respective SAPS 3 scores (Fig. 3a), any degree of AKI resulted in an pronounced excess mortality. Standardized mortality ratios were equally increased for both AKIN stage 1 and 2 (1.17 and 1.16, respectively) with a further rise in stage 3 (1.31). Logistic regression including SAPS 3 corrected by serum creatinine shows significantly increased odds ratio for death (Table 4).

AKI defined by RIFLE

Using RIFLE within the first 2 days of ICU admission 5,093 patients (35.5%) were classified as AKI with a maximum RIFLE category: Risk in 7.6%, Injury in 11.1% and Failure in 16.8% (Fig. 1). More pronounced severity of AKI as classified by RIFLE was associated with increased hospital mortality (Table 5). The respective survival curves are shown in Fig. 2b.

Demographic data for each RIFLE class are presented in ESM (Table E2).

Increasing degree of AKI resulted in an enhanced excess mortality when compared to mortalities expected by respective SAPS 3 Scores (Fig. 3b). Logistic regression including SAPS 3 corrected by serum-creatinine as

well as the RIFLE classes shows significantly increased odds for non-survival (Table 6).

Influence of UO on primary outcome

Stability of UO allocation was checked by sensitivity analysis (ESM Table E3).

In both classification systems mortalities observed for each degree of AKI based on worst UO alone appeared to be slightly lower than the same stage of injury characterized by the standard definition (Tables 3, 5). However, classification of AKI using only worst creatinine resulted in clearly higher mortality rates at each stage as compared to categorization by either the UO or the composite criteria.

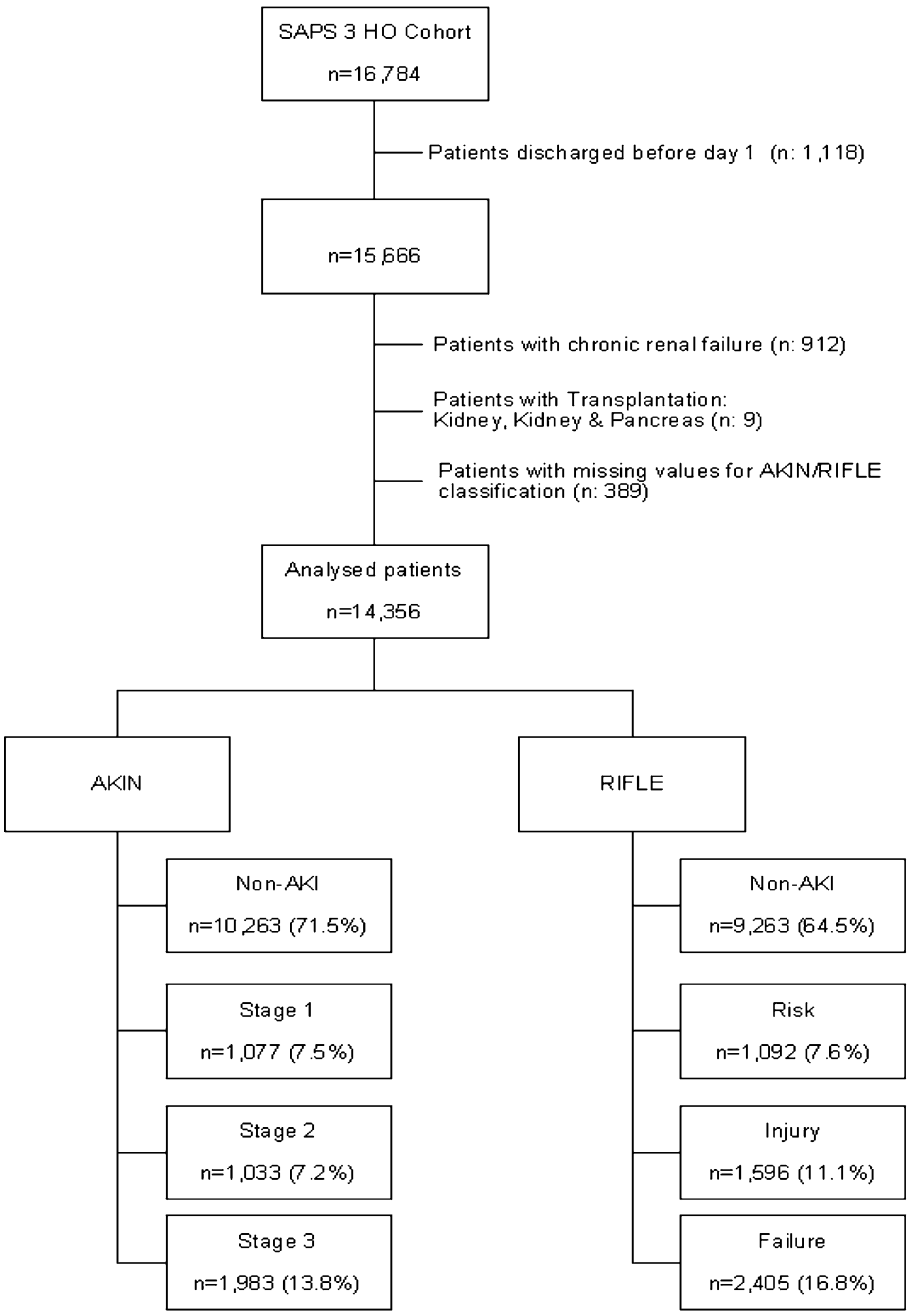

Fig. 1 Study flow chart

Table 2 Patient demographics, outcome and comorbidities at ICU admission for the entire cohort

	Cohort	
	n	%
Number of patients	14,356	100.00
Female gender	5,631	39.20
Age, years (median Q1–Q3)	63	49.00–74.00
ICU LOS, days (median Q1–Q3)	2.80	1.10–6.70
s-Creatinine on admission, mg/dl (median Q1–Q3)	1.0	0.8–1.3
ICU admission status		
Planned	4,950	34.50
Unplanned	9,089	63.30
Missing	317	2.20
Surgical status		
No surgical procedure	6,052	42.20
Scheduled surgery	5,101	35.50
Emergency surgery	2,516	17.50
Missing	687	4.80
Risk adjustment		
SOFA score (median Q1–Q3)	3.00	2.00–6.00
SAPS 3 score (median Q1–Q3)	47.00	37.00–59.00
Outcome		
ICU mortality (%)		16.00
Hospital mortality (%)		21.70
O/E ratio + 95% CI	0.97	0.94–0.99
Comorbidities		
Arterial hypertension	5,019	35.00
Chronic heart failure		
Class II NYHA	710	4.90
Class III NYHA	443	3.10
Class IV NYHA	157	1.10
Chronic pulmonary failure	601	4.20
Cirrhosis	444	3.10
COPD	1,812	12.60
Diabetes		
Insulin-dependent	392	2.70
Non-insulin-dependent	837	5.80
Cancer		
Metastatic cancer	430	3,00
Non-metastatic cancer	880	6,10

Comparison of classification according to AKIN versus RIFLE

The number of patients categorized as AKI differed by roughly 1,000 (7%) between the two systems (Fig. 1). By cross tabulating the stages obtained by either RIFLE or AKIN (Table 7) it became obvious that 1,504 patients (10.5%) classified as non-AKI by AKIN were classified as AKI by RIFLE, roughly half of them fell into the Risk category. These patients did not show an increase in serum creatinine of at least 0.3 mg/dl within 48 h. Mortality of this group of patients was clearly increased ranging from 27.7% (Risk) to 41.2% (Failure) as compared to 12.9% for patients classified as non-AKI by both systems.

On the other hand 504 patients (3.5%) classified as non-AKI by RIFLE were categorized as AKI by the AKIN criteria, nearly all of them belonging to stage 1 ($n = 457$). This group consisted of patients showing either a low serum creatinine (<0.8 mg/dl) on ICU admission ($n = 249$) or classifying for AKIN stage 1 by the 0.3 mg/dl serum creatinine increase criterion ($n = 208$). Mortality of this group was about twice that of patients classified as non-AKI by both AKIN and RIFLE (25.2 vs. 12.9%, respectively).

Altogether 596 patients (4.1%) showed an increase in serum creatinine ≥0.3 mg/dl as the only criterion for AKI. The respective RIFLE classes assigned to these patients were non-AKI ($n = 208$), Risk ($n = 160$), Injury ($n = 159$) and Failure ($n = 69$).

Mortality rates in each RIFLE class were increased by 5.3% (Risk) to 18.7% (Failure) when patients also fulfilled the criteria of AKIN stage 1 as compared to AKIN non-AKI.

Discussion

There is wide agreement that a generally applicable classification system is required for AKI which helps to standardize estimation of severity of renal dysfunction and to predict outcome associated with this condition [6, 19]. After the introduction of the RIFLE criteria several years ago [3], a modification was published very recently by AKIN introducing a dynamic application [11]. This is currently the largest study comparing the performance of these two classification systems by applying the proposed

Table 3 Hospital mortality of AKI stages according to AKIN criteria: hospital mortalities were calculated separately for patients according to their urinary output or their serum creatinine changes alone and the combination of both criteria

AKIN	Creatinine or urinary output criterion (=standard definition)			Urinary output criterion (alone)			Creatinine criterion (alone)		
	Total (*n*)	Died (*n*)	HM (%)	Total (*n*)	Died (*n*)	HM (%)	Total (*n*)	Died (*n*)	HM (%)
Non-AKI	10,263	1,630	15.9	10,816	1,938	17.9	11,623	2,106	18.1
Stage 1	1,077	372	34.5				1,463	589	40.3
Stage 2	1,033	300	29.0	941	273	29.0	202	101	50.0
Stage 3	1,983	817	41.2	1,837	753	41.0	262	138	52.7

HM hospital mortality

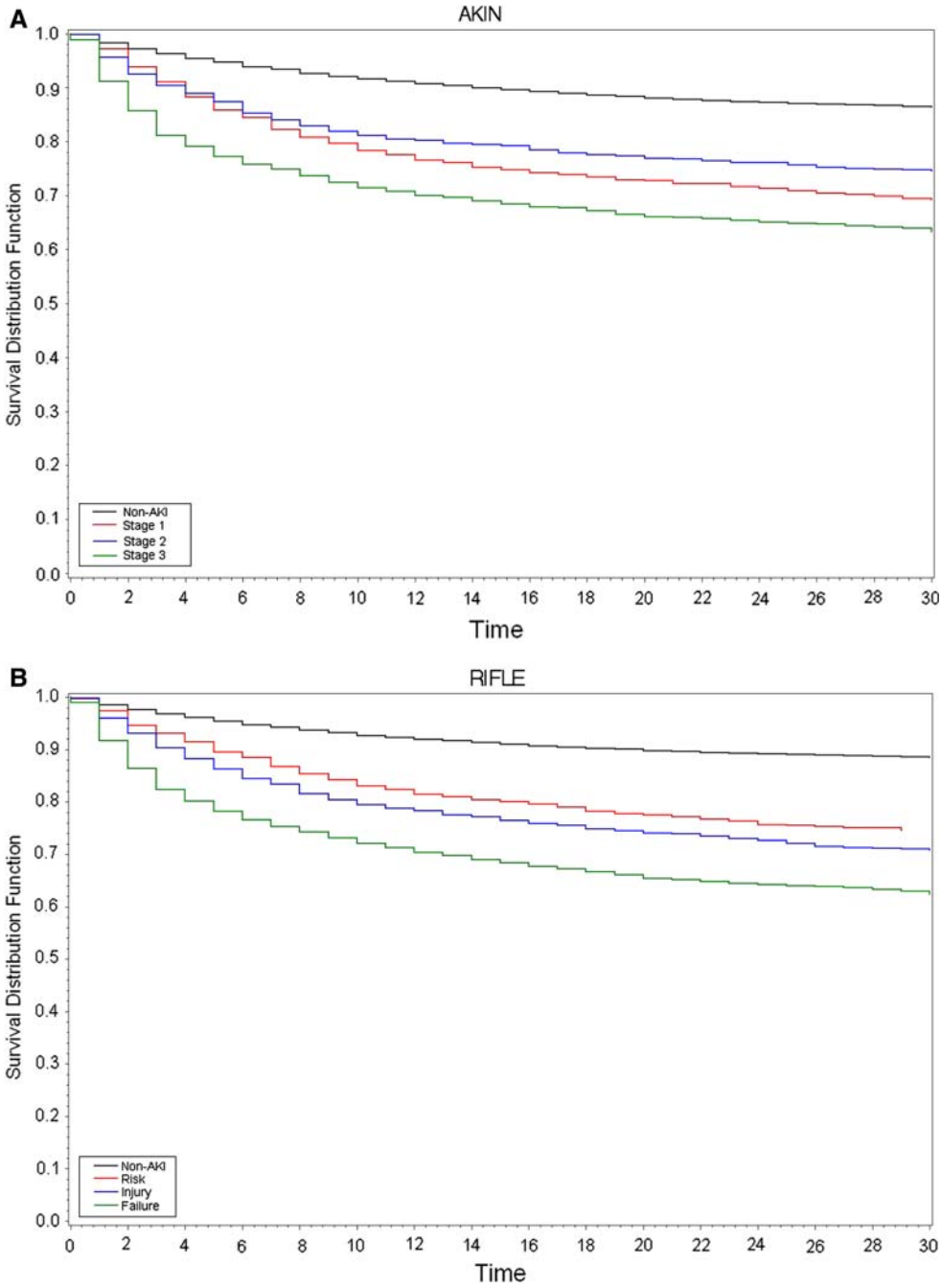

Fig. 2 Survival curve (30 days) of patients classified according to AKIN (**a**) or RIFLE (**b**) time = days

48 h window to define severity of AKI by stages according to AKIN. By analysing >14,000 patients admitted to various ICUs over the world, we found that AKI occurring within the first 2 days after admission was associated with increased mortality. We could further demonstrate that any stage of acute renal impairment was independently and strongly predictive of increased odds for death. When comparing AKIN criteria with the more established RIFLE criteria, we found some inherent differences in classification despite similar performance with regard to predicting outcome.

The AKIN classification proposes an observation period of 48 h for the defined changes in each stage of AKI to occur, providing a measure of acuity which can be used for differentiation from slow changes in renal function occurring over longer periods. Additionally, by this definition changes in renal function may be determined independently of the baseline creatinine values.

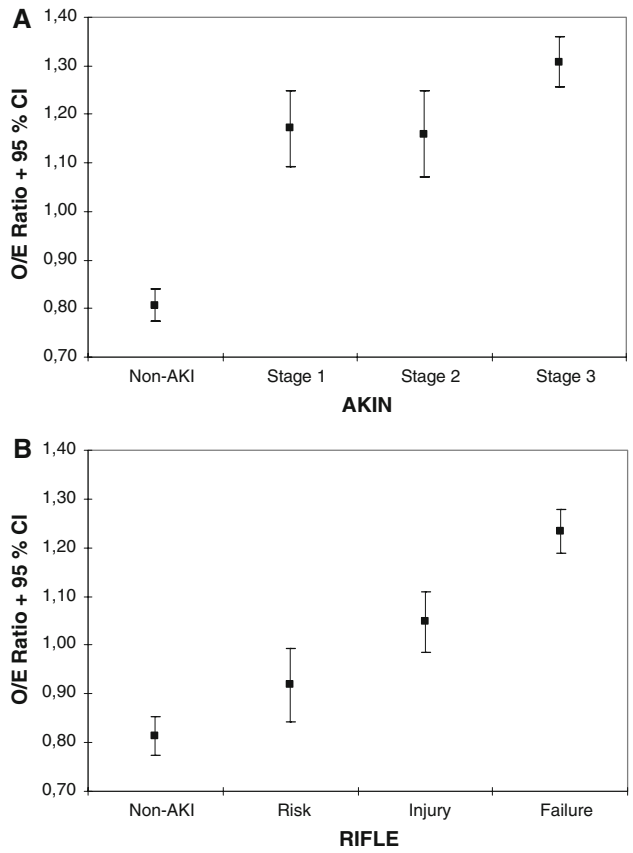

Fig. 3 Standardized mortality (observed-to-expected mortality) ratios of acute kidney injury classified by AKIN (**a**) or RIFLE (**b**). Vales are mean ± 95% confidence interval

Table 4 Logistic regression for AKIN including SAPS 3 corrected by serum creatinine

Effect	Odds ratio	95% Confidence interval	*P* value
AKI: stage 1	2.07	1.77–2.43	<0.001
AKI: stage 2	1.93	1.63–2.28	<0.001
AKI: stage 3	2.99	2.64–3.38	<0.001
SAPS $3_{corrected}$	1.10	1.09–1.10	<0.001

Odds ratio for hospital death
SAPS $3_{corrected}$: SAPS 3 score corrected by serum creatinine
Area under the receiver operating characteristic curve 0.845; R^2 0.247; maximum rescaled R^2 0.380

We clearly demonstrated that any stage of AKI is associated with significantly increased mortality as compared to those patients classified as "non-AKI" by UO and a lack of significant increase in serum creatinine within 48 h. This information is important because it demonstrates that changes in renal function after admission to the ICU must be considered significant. It is noteworthy that about 50% of the patients assigned to AKIN stage 1 were classified by the recently introduced condition of an increase in serum creatinine of more than 0.3 mg/dl [11] but less than 150% from admission value. This reflects the findings of several recent investigations demonstrating a clear association between small dynamic changes in serum creatinine and increased hospital mortality [5, 20, 21].

Even after controlling for confounding factors by using logistic regression analysis using SAPS 3 as a measure for severity of diseases, the AKIN stages 1, 2 and 3 remained independent risk factors for hospital mortality which was also reflected by the increased O/E mortality ratios of each stage.

Somewhat unexpected was the finding that O/E mortality ratio of stage 1 was considerably increased and equal to that of stage 2. This nonlinear relationship between O/E mortality ratios and AKI stage may be partly explained by the influence of the UO criterion as applied in our study. Since our database does not track UO at 6-h intervals, but only at 24-h intervals, we could not distinguish between the AKIN stage 1 and 2 subgroups by this parameter. Under the assumption that the requirement of the UO to be less than 0.5 ml/kg/h for 24 h is more stringent than for 6 h, we assigned these patients to stage 2. As demonstrated by sensitivity analysis, this resulted also in less serious cases being assigned to the more serious subgroup and decreasing overall mortality in stage 2. Although assigning UO in the same way to the Injury category, this lack of linearity could not be observed for the RIFLE classification. This implies a different impact of the creatinine criterion on AKIN stages as compared to RIFLE stages, which is also reflected by mortalities differing between the corresponding stages of both systems when only creatinine criteria are applied. Several explanations may be provided for this finding. First, the dynamic definition of AKI per se leads to some distortion in the distribution between stages 2 and 3 depending on the serum creatinine values at the beginning of the 48-h observation period. For instance, starting from a serum creatinine of 2 mg/dl and increasing to 4.4 mg/dl, a patient would not classify as stage 2 despite the relative increase to >200%, but rather as stage 3, because end creatinine is greater than 4 mg/dl with an increase ≥0.5 mg/dl. Secondly, a different assignment of patients with serum creatinine ≥4.0 mg/dl by the AKIN criteria as compared to RIFLE can be observed. Both systems require an increase of ≥0.5 mg/dl for these patients to classify for stage 3 or Failure, respectively. However, if they show an increase which is less than 0.5 mg/dl but ≥0.3 mg/dl within 48 h, then AKIN classification will assign them to stage 1 despite having a significant degree of renal failure associated with higher mortality. Finally, it must be pointed out that we could not include RRT for staging of AKIN, which may have resulted in classification of patients into lower stages based on their serum creatinine or UO instead of stage 3 because of needing RRT.

Table 5 Hospital mortality of AKI stages according to RIFLE criteria: hospital mortalities were calculated separately for patients according to their urinary output or their serum creatinine changes alone and the combination of both criteria

RIFLE	Creatinine or urinary output criterion (=standard definition)			Urinary output criterion (alone)			Creatinine criterion (alone)		
	Total (*n*)	Died (*n*)	HM (%)	Total (*n*)	Died (*n*)	HM (%)	Total (*n*)	Died (*n*)	HM (%)
Non-AKI	9,263	1,261	13.6	10,816	1,938	17.9	10,744	1,562	14.5
Risk	1,092	319	29.2				1,436	473	32.9
Injury	1,596	515	32.3	941	273	29.0	1,061	495	46.7
Failure	2,405	1,024	42.6	1,837	753	41.0	962	542	56.3

HM hospital mortality

Table 6 Logistic regression for RIFLE including SAPS 3 corrected by serum creatinine

Effect	Odds ratio	95% Confidence interval	*P* value
RIFLE: risk	1.38	1.17–1.63	0.001
RIFLE: injury	1.90	1.65–2.18	<0.001
RIFLE: failure	2.99	2.66–3.36	<0.001
SAPS $3_{corrected}$	1.09	1.09–1.10	<0.001

Odds ratio for hospital death
SAPS $3_{corrected}$: SAPS 3 score corrected by serum creatinine
Area under the receiver operating characteristic curve 0.845; R^2 0.247; maximum rescaled R^2 0.380

As with several prior studies [7–9, 22], we could establish a clear correlation between the degree of AKI defined by RIFLE and mortality. RIFLE classification relies on prior knowledge of the baseline creatinine [3]. If unavailable, it is suggested that the initial serum creatinine is calculated by the MDRD formula assuming a GFR of at least 75 ml/min/1.72 m^2 [3, 23, 24]. Though most studies investigating RIFLE used a mixture of available and estimated baseline serum creatinines [8, 9, 25, 26], the feasibility of using exclusively MDRD-derived baseline values has recently been demonstrated [9, 10, 13, 27]. We used the same approach, which seems reasonable because we had excluded all patients with chronic renal failure from analysis beforehand. Nevertheless, it cannot be ruled out that some misclassification of patients with chronic kidney disease may have occurred by applying estimated, instead of real, baseline creatinine values, contributing to the finding that more patients were classified as AKI by RIFLE than by AKIN. As already mentioned, patients with UO <0.5 ml/kg/h were assigned to RIFLE Injury. In contrast to the AKIN classification, this approach resulted in a linear relationship between O/E mortality ratios and the degrees of AKI. This may be explained by the significantly higher number of patients which were classified into Injury and Failure by serum creatinine. Apparently RIFLE captured more pre-existing AKI because of baseline function imputation. Therefore RIFLE was less subject to the effects of the urine output criterion.

An interesting finding of our investigation was the relative contribution of each criterion to mortality in both classification systems. The introduction of the urine output criterion into RIFLE (and its modification by AKIN) was thought to increase sensitivity [3, 7]. However, concerns about the reliability of this parameter were raised due to its dependency on "extrarenal" factors such as volume status or release of antidiuretic hormone [28, 29]. In our study, mortality rates of AKI stages defined by worst UO were consistently lower than when defined by worst serum creatinine. Consequently, though increasing the number of patients classifying as AKI, inclusion of UO reduced mortality when using the standard definition (urine output or creatinine). Thus, UO appears a very sensitive parameter carrying, however, a lower mortality in the respective stages as reported also by other authors [7, 8, 12, 30].

Finally, direct comparison of the two classification systems revealed shortcomings on both sides. First of all RIFLE appeared to classify roughly 7% more patients as having AKI. These were mainly those patients who presented with significantly increased serum creatinine values as compared to the estimated baselines which did not further increase during the 48-h observation period. These patients had two to threefold increased mortalities compared to those patients classified as non-AKI by both systems and, consequently, must be considered as misclassified by AKIN. On the other hand, roughly 500 patients showing an increase of the serum creatinine ≥0.3 mg/dl within 48 h did not reach the limit of a 50% increase in serum creatinine from calculated baseline and, consequently, were classified as non-AKI by RIFLE. This group also showed a nearly twofold increase in mortality as compared to the group without AKI and, therefore, must be regarded as misclassified by RIFLE. Furthermore, in each RIFLE class the mortality of patients also fulfilling the criteria of AKIN stage 1 was distinctively higher than the mortality of those patients who did not present a relevant increase in serum creatinine within 48 h, which highlights the importance of the dynamic component of the AKIN definition.

Our results are different from two recent investigations which could not find a significant difference between these two classification systems [13, 14]. The study by

Table 7 Cross tabulation of patients classified by AKIN versus RIFLE

AKIN		RIFLE					Total (AKIN)
		non-AKI	Risk	Injury	Failure		
non-AKI	n *	**8759** ***(12.9%)***	781 *(27.7%)*	452 *(37.4%)*	271 *(41.3%)*		10263 *(15.9%)*
Stage 1	n *	457 *(25.2%)*	**282** ***(33.0%)***	243 *(44.0%)*	95 *(60.0%)*		1077 *(34.5%)*
Stage 2	n *	36 *(30.6%)*	21 *(47.6%)*	**885** ***(25.9%)***	91 *(54.9%)*		1033 *(29.0%)*
Stage 3	n *	11 *(18.2%)*	8 *(12.5%)*	16 *(62.5%)*	**1948** ***(41.3%)***		1983 *(41.2%)*
Total (RIFLE)	n *	9263 *(13.6%)*	1092 *(29.2%)*	1596 *(32.3%)*	2405 *(42.6%)*		**14356** ***(21.7%)***

Number of patients classified into the respective stages of AKI by AKIN or RIFLE are cross-tabulated against each other. Hospital mortality of each group is given in brackets. Fields marked in yellow denominate patients assigned to the same degree of AKI by both classification systems

n number of patients

[a] Hospital mortality rate (%) of the respective group

Bagshaw and colleagues [13], however, applied only a 24-h observation period and referred both RIFLE and AKIN criteria to the calculated baselines which eliminates the major difference between those two systems, i.e. the dynamic change over a 48-h time period. Lopes and colleagues [14], on the other hand, used the lowest serum creatinine available within a 48-h observation period for AKIN classification, which does not comply with the original publication [11] and results in patients with falling creatinine being (mis)classified as AKI. This approach may also explain their unusually high incidence rate for AKI of 50%, which is much higher than the roughly 30% described both in large retrospective analyses [4, 28] and in recent investigations using the new AKIN definition in a very similar population [15, 31].

Our study has several limitations: First, UO was not collected in 6-h intervals, obviating the use of this parameter to define AKIN stage 1 or RIFLE Risk, respectively. As outlined above, this may have resulted in classifying patients with less severe AKI into the intermediate degree of AKI. Also, patients classifying for AKIN stage 1 or RIFLE Risk may have been missed entirely, if, for example, they had a UO of <0.5 ml/kg/hr for only 6 h but a UO greater than that for the following 18 h. However, both situations should have affected AKIN and RIFLE the same way.

Secondly, since we did not have baseline serum creatinine values from our patients, we used estimate baselines calculated by the MDRD equation. Although this may have resulted in some misclassification within the RIFLE system, O/E mortality ratios showed perfect correlation with increasing degrees of AKI.

Finally, the requirement of RRT was not available from the SAPS 3 database, obviating both its inclusion as a renal endpoint into our analysis and evaluation of its influence as a newly introduced criterion for stage 3 on the performance of the AKIN classification. However, our analysis excluded patients with chronic renal failure and was restricted to the first 48 h of ICU admission. Since the average time to start RRT after ICU admission is reported to be between 1.2 and 6 days, the effect of this limitation may be very moderate [23, 32, 33].

In conclusion, AKI can be identified in more than 28% of ICU patients during the first 48 h of admission. Each stage of AKI is associated with increased mortality. A direct comparison between AKIN and RIFLE criteria

indicates that both the degree of increase from baseline and the dynamic aspect (i.e. the rate of rise) are relevant for staging and prognosis. Misclassification of AKI occurs by both classification systems, but clearly less frequently by RIFLE classification. Even when taking the shortcomings of our study design into account RIFLE demonstrates higher sensitivity as well as better robustness in predicting the outcome of AKI. Further prospective trials will be required to answer questions about necessary modifications which should combine the advantages of both systems.

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Conflict of interest statement None.

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