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The primary aim of *World Journal of Clinical Cases* (*WJCC*, *World J Clin Cases*) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

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ORIGINAL ARTICLE

Retrospective Study

Acute kidney injury in traumatic brain injury intensive care unit patients

Zheng-Yang Huang, Yong Liu, Hao-Fan Huang, Shu-Hua Huang, Jing-Xin Wang, Jin-Fei Tian, Wen-Xian Zeng, Rong-Gui Lv, Song Jiang, Jun-Ling Gao, Yi Gao, Xia-Xia Yu

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Abstract

BACKGROUND

The exact definition of Acute kidney injury (AKI) for patients with traumatic brain injury (TBI) is unknown.

AIM

To compare the power of the "Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease" (RIFLE), Acute Kidney Injury Network (AKIN), Creatinine kinetics (CK), and Kidney Disease Improving Global Outcomes (KDIGO) to determine AKI incidence/stage and their association with the in-hospital mortality rate of patients with TBI.

METHODS

This retrospective study collected the data of patients admitted to the intensive care unit for neurotrauma from 2001 to 2012, and 1648 patients were included. The subjects in this study were assessed for the presence and stage of AKI using RIFLE, AKIN, CK, and KDIGO. In addition, the propensity score matching method was used.

RESULTS

Among the 1648 patients, 291 (17.7%) had AKI, according to KDIGO. The highest incidence of AKI was found by KDIGO (17.7%), followed by AKIN (17.1%), RIFLE

(12.7%), and CK (11.5%) (P = 0.97). Concordance between KDIGO and RIFLE/AKIN/CK was 99.3%/99.1%/99.3% for stage 0, 36.0%/91.5%/44.5% for stage 1, 35.9%/90.6%/11.3% for stage 2, and 47.4%/89.5%/36.8% for stage 3. The in-hospital mortality rates increased with the AKI stage in all four definitions. The severity of AKI by all definitions and stages was not associated with in-hospital mortality in the multivariable analyses (all P > 0.05).

CONCLUSION

Differences are seen in AKI diagnosis and in-hospital mortality among the four AKI definitions or stages. This study revealed that KDIGO is the best method to define AKI in patients with TBI.

Key Words: Kidney Disease Improving Global Outcomes; Acute Kidney Injury; Traumatic brain injury; Evaluation; In-hospital mortality

Core Tip: Because the exact definition of Acute Kidney Injury (AKI) for patients with Traumatic brain injury (TBI) is unknown, this study compared the power of four different AKI diagnose criteria to determine AKI incidence/stage and their association with the in-hospital mortality rate of patients with TBI.

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INTRODUCTION

Traumatic brain injury (TBI) is a debilitating condition that can be exacerbated by the co-occurrence of acute kidney injury (AKI), which is a clinical syndrome characterized by the abrupt loss of the kidney's excretory function and is often combined with oliguria. The development of AKI usually occurs over the course of hours to days[1]. AKI is observed in 9% of the patients with TBI, and 42% of those patients die in the hospital[2]. Thus, early identification and subsequent clinical intervention of AKI in TBI patients are critical to survival[3].

Nevertheless, it is difficult to determine the true incidence and outcomes of AKI due to the use of different validation criteria[4-6]. The reported incidence of AKI varies greatly, ranging from 15% to 74.2%[7-10]. Moreover, serum creatinine (SCr) and urine output (UO) in patients with TBI are greatly impacted by muscle injury or breakdown secondary to decreased perfusion pressure and the use of osmotic diuretics like mannitol[4-6]. Therefore, sensitive and reliable criteria for AKI are needed for diagnosis and staging, especially in TBI patients.

Since 2004, at least four different AKI definitions and criteria have been proposed. The "Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease" (RIFLE) classification was the first validated tool for AKI identification[11]. It is based on SCr levels and UO and defines three severity classes of AKI (risk, injury, and failure) and two outcome classes (Loss of kidney function and End-stage kidney disease). Following that, the Acute Kidney Injury Network (AKIN) criteria were proposed in 2007 as a modification of the RIFLE criteria[12]. The AKIN is based on evidence that suggests that even small increases in SCr are associated with a poor outcome. It is also based on SCr and UO and defines three stages (1, 2, and 3). Following the evidence for small changes in SCr and outcomes, the creatinine kinetics (CK) model was proposed by Waikar and Bonventre[13], who defined AKI based on the absolute changes in baseline SCr levels over 24-48 h. In 2012, an updated consensus definition of AKI was further proposed by the Kidney Disease Improving Global Outcomes (KDIGO) group to reconcile the subtle differences in the RIFLE and AKIN criteria and to establish a common definition known as the KDIGO criteria[14]. Nevertheless, currently, there are no widely accepted criteria to determine the severity of AKI for patients with TBI in the intensive care unit (ICU)[2,7,15], and the power of the criteria above among TBI patients' needs further exploration.

Therefore, the present study aimed to explore the compatibility among the RIFLE, AKIN, CK, and KDIGO definitions, and to compare the power of these criteria in determining the incidence and stage of AKI and explore the association between severity of AKI by all definitions/stages and in-hospital mortality of patients admitted to ICU for TBI.

Table 1 Patient characteristics according to the Kidney Disease Improving Global Outcomes criteria (propensity score matching)

Characteristics	Total patients (*n* = 582)	Non-AKI (*n* = 291)	AKI (*n* = 291)	*P* value
Ethnicity				0.195
White	415 (71.3)	206 (70.8)	209 (71.8)	
Hispanic/Latino	8 (1.4)	7 (2.4)	1 (0.3)	
African American	22 (3.8)	13 (4.5)	9 (3.1)	
Asian	3 (0.5)	2 (0.7)	1 (0.3)	
Other/unknown	134 (23.0)	63 (21.7)	71 (24.4)	
Age (yr)	55.3 ± 23.9	54.7 ± 24.7	55.8 ± 23.1	0.595
Sex				0.925
Female	152 (26.1)	75 (25.8)	77 (26.5)	
Male	430 (73.9)	216 (74.2)	214 (73.5)	
Elixhauser score	8.1 ± 11.5	7.4 ± 10.9	8.7 ± 12.1	0.187
SAPS II	34.8 ± 14.8	33.1 ± 13.4	36.6 ± 15.9	0.004
SOFA	4.4 ± 2.9	4.0 ± 2.7	4.8 ± 3.1	0.001
GCS	12.8 ± 3.2	12.8 ± 3.2	12.9 ± 3.3	0.778
Craniotomy	84 (14.4)	42 (14.4)	42 (14.4)	> 0.99
Peak SCr (μmol/L)	1.46 ± 0.72	1.22 ± 0.34	1.70 ± 0.90	< 0.001
SCr at admission (μmol/L)	1.19 ± 0.46	1.08 ± 0.27	1.29 ± 0.57	< 0.001
Use of antiplatelet drugs	40 (6.87)	16 (5.50)	24 (8.25)	0.251
Use of anticoagulants	13 (2.2)	5 (1.7)	8 (2.8)	0.575
Use of vancomycin	178 (30.6)	80 (27.5)	98 (33.7)	0.126
Use of ARB/ACE-I	34 (5.8)	19 (6.5)	15 (5.2)	0.596
Use of aminoglycosides	39 (6.7)	16 (5.5)	23 (7.9)	0.320
Transfusion (mL)	553 ± 1589	400 ± 1077	645 ± 1967	0.063
Red blood cell (mL)	276 ± 1109	174 ± 623	377 ± 1433	0.027
Plasma (mL)	232 ± 690	214 ± 646	250 ± 733	0.526
Shock	177 (30.4)	73 (25.1)	104 (35.7)	0.007
UO (mL)	0.68 ± 0.60	0.70 ± 0.44	0.67 ± 0.73	0.468

Data are shown as *n* (%) or mean ± SD. *P* values < 0.05 were considered statistically significant. KDIGO: Kidney Disease Improving Global Outcomes; PSM: Propensity score matching; AKI: Acute kidney injury; SAPS II: Simplified acute physiology score; SOFA: Sequential organ failure assessment; GCS: Glasgow coma scale; Scr: Serum creatinine; ARB: Angiotensin receptor blocker; ACE-I: Angiotensin-converting enzyme inhibitor; UO: Urine output.

MATERIALS AND METHODS

Subjects

This was a retrospective study of patients admitted to the ICU for neurotrauma from 2001 to 2012. The exclusion criteria were: (1) Discharged within 24 h; or (2) < 18 years of age; or (3) missing data; or (4) history of end-stage renal disease (ESRD). The patients were included in the AKI and non-AKI groups according to whether they were diagnosed with AKI based on the KDIGO criteria[16].

The data for this study were extracted from the Medical Information Mart for Intensive Care (MIMIC-III, https://mimic.physionet.org/about/mimic/). It is a large public single-center database[17] that contains information relating to patients admitted to the critical care units at Beth Israel Deaconess Medical Center during 2001-2012. The presence of TBI was defined by diagnostic code, ICD-9, in MIMIC-III[18].

This retrospective study was approved by the Ethics Committee for Human Research of Shenzhen Hospital, Southern Medical University (No. NYS2YYEC20180009), which waived the requirement for informed consent from subjects.

Table 2 Patient characteristics by Kidney Disease Improving Global Outcomes stage before propensity score matching

Characteristics	Total patients (*n* = 1648)	Non-AKI (*n* = 1357)	AKI (*n* = 291)	*P* value
Ethnicity				0.070
White	1220 (74.0)	1011 (74.5)	209 (71.8)	
Hispanic/Latino	20 (1.2)	19 (1.4)	1 (0.3)	
African American	55 (3.3)	46 (3.4)	9 (3.1)	
Asian	23 (1.4)	22 (1.6)	1 (0.3)	
Other/unknown	330 (20.0)	259 (18.8)	71 (28.4)	
Age (yr)	58.5 ± 22.5	59.0 ± 22.4	55.8 ± 22.1	0.025
Sex				0.001
Female	603 (36.6)	526 (38.8)	77 (26.5)	
Male	1045 (63.4)	831 (61.2)	214 (73.5)	
Elixhauser score	6.4 ± 10.2	5.9 ± 9.6	8.7 ± 12.1	< 0.001
SAPS II	31.9 ± 13.0	30.9 ± 12.0	36.6 ± 15.9	< 0.001
SOFA	3.3 ± 2.5	2.9 ± 2.2	4.8 ± 3.1	< 0.001
GCS	13.1 ± 2.9	13.1 ± 2.8	12.9 ± 3.3	0.096
Craniotomy	344 (20.9)	302 (22.3)	42 (14.4)	0.020
Peak SCr (μmol/L)	1.09 ± 0.53	0.96 ± 0.27	1.70 ± 0.90	< 0.001
SCr at admission (μmol/L)	0.95 ± 0.36	0.88 ± 0.23	1.29 ± 0.57	< 0.001
Use of antiplatelet drugs	138 (8.4)	114 (8.4)	24 (8.3)	0.932
Use of anticoagulants	31 (1.9)	23 (1.7)	8 (2.8)	0.235
Use of vancomycin	408 (24.8)	310 (22.8)	98 (33.7)	< 0.001
Use of ARB/ACE-I	84 (5.1)	69 (5.1)	15 (5.2)	0.961
Use of aminoglycosides	80 (4.9)	57 (4.2)	23 (7.9)	0.008
Transfusion (mL)	309 ± 1082	237 ± 752	645 ± 1967	0.001
Red blood cell (mL)	141 ± 710	93 ± 398	377 ± 1433	0.001
Plasma (mL)	158 ± 596	138 ± 560	250 ± 733	0.004
Shock	460 (27.9)	356 (26.2)	104 (35.7)	< 0.001
UO (mL)	0.80 ± 1.06	0.83 ± 1.12	0.67 ± 0.73	0.016

Data are shown as *n* (%) or mean ± SD. *P* values < 0.05 were considered statistically significant. KDIGO: Kidney Disease Improving Global Outcomes; PSM: Propensity score matching; AKI: Acute kidney injury; SAPS II: Simplified acute physiology score; SOFA: Sequential organ failure assessment; GCS: Glasgow coma scale; Scr: Serum creatinine; ARB: Angiotensin receptor blocker; ACE-I: Angiotensin-converting enzyme inhibitor; UO: Urine output.

Data collection

Demographics and clinical data were retrieved for all patients, including sex, age, ethnicity, category diagnosis at ICU admission, Elixhauser score, simplified acute physiology score (SAPS II), SOFA score, Glasgow Coma Scale (GCS) score[19], serum creatinine concentration (SCr), including peak SCr and SCr at admission, previous treatment (craniotomy, transfusion and the use of antiplatelet drugs, anticoagulants, vancomycin, angiotensin receptor blocker/angiotensin-converting enzyme inhibitor (ARB/ACE-I) and aminoglycosides), length of stay (in days), UO, APACHE II classification, and in-hospital, 30-d, and 1-year mortality rates. Comorbidity was defined and calculated using the ICD-9-CM codes based on Elixhauser's algorithm[20]. Patients presenting with shock upon admission, organ failure, and multiple organ failure (MOF) were selected according to definitions previously published [21].

If the patient's weight value was missing, the patient's height was used to estimate the weight[22]. Based on baseline SCr, the two groups in this study were assessed for the presence and stage of AKI using RIFLE[11], AKIN[12], CK[13], and KDIGO[16]. Baseline SCr was calculated according to the theoretical baseline SCr value for a given patient, assuming normal GFR[11].

Table 3 Patient characteristics by Kidney Disease Improving Global Outcomes stage

Characteristics	Stage 1 (*n* = 200)	Stage 2 (*n* = 53)	Stage 3 (*n* = 38)	*P* value
Ethnicity				0.512
White	141 (70.5)	39 (73.6)	29 (76.3)	
Hispanic/Latino	1 (0.5)	0	0	
African American	5 (2.5)	3 (5.7)	1 (2.6)	
Asian	1 (0.5)	0	0	
Other/unknown	52 (26.0)	11 (20.8)	8 (21.1)	
Age (yr)	53.4 ± 23.1	64.6 ± 20.4	55.8 ± 23.9	0.001
Sex				< 0.001
Female	42 (21.0)	23 (43.4)	12 (31.6)	
Male	158 (79.0)	30 (56.6)	26 (68.4)	
Elixhauser score	8.2 ± 12.5	8.9 ± 9.9	11.1 ± 12.9	< 0.001
SAPS II	35.1 ± 16.0	39.2 ± 12.8	40.6 ± 18.1	< 0.001
SOFA	4.6 ± 2.9	4.6 ± 2.9	6.3 ± 4.0	< 0.001
GCS	12.9 ± 3.3	12.9 ± 3.2	12.7 ± 3.8	0.582
Craniotomy	28 (14.0)	7 (13.2)	7 (18.4)	0.025
Max creatinine (μmol/L)	1.49 ± 0.44	1.70 ± 1.03	2.81 ± 1.54	< 0.001
Creatinine at admission (μmol/L)	1.24 ± 0.34	1.22 ± 0.57	1.67 ± 1.14	< 0.001
Use of antiplatelet drugs	94 (9.8)	20 (13.2)	10 (13.0)	0.890
Use of anticoagulant	21 (2.2)	8 (5.3)	5 (6.49)	0.281
Use of vancomycin	74 (37.0)	14 (26.4)	10 (26.32)	< 0.001
Use of ARB/ACE-I	9 (4.5)	5 (9.4)	1 (2.63)	0.443
Use of aminoglycosides	14 (7.0)	5 (9.4)	4 (10.53)	0.040
Transfusion (mL)	537 ± 1081	500 ± 1210	1412 ± 4613	< 0.001
Red blood cell (mL)	291 ± 692	274 ± 920	974 ± 3451	< 0.001
Plasma (mL)	231 ± 666	213 ± 606	400 ± 1133	0.010
Shock	460 (26.9)	356 (26.2)	104 (35.74)	0.004
UO (mL)	0.70 ± 0.80	0.62 ± 0.47	0.53 ± 0.58	0.080

Data are shown as *n* (%) or mean ± SD. *P* values < 0.05 were considered statistically significant. KDIGO: Kidney Disease Improving Global Outcomes; PSM: Propensity score matching; AKI: Acute kidney injury; SAPS II: Simplified acute physiology score; SOFA: Sequential organ failure assessment; GCS: Glasgow coma scale; Scr: Serum creatinine; ARB: Angiotensin receptor blocker; ACE-I: Angiotensin-converting enzyme inhibitor; UO: Urine output.

Statistical analysis

The matching factors for propensity score matching (PSM) were ethnicity, age, sex, Elixhaouser score, SAPS II, SOFA, GCS, craniotomy, max creatinine, creatinine at admission, use of antiplatelet drugs, use of anticoagulants, shock, use of vancomycin, use of ARB/ACE-I, use of aminoglycosides, transfusion, red blood cell, plasma, and UO. The matching ratio was 1:1. Statistical analyses were performed using STATA 12.0 (StataCorp LP, College Station, TX, United States). The continuous data were tested for normal distribution using the Kolmogorov-Smirnov test. Those with a normal distribution were presented as means ± SD and analyzed using Student's *t*-test; otherwise, they were presented as medians [interquartile ranges (IQR)] and analyzed using the Mann-Whitney *U*-test. The categorical data were presented as numbers (percentages) and analyzed using the chi-square test or Fisher's exact test. Univariable and multivariable (enter) logistic regression analyses were performed to explore the association between in-hospital mortality (dependent variable) and the AKI stages diagnosed by CK, RIFLE, AKIN, and KDIGO. In-hospital, 30-d, and 1-year mortality rates were analyzed using the Kaplan-Meier method and the log-rank test. The observed proportional agreement was used to examine the compatibility between the different scoring systems. The Marascuilo procedure was used for multiple comparisons. Two-sided *P* values < 0.05 were considered statistically significant.

Table 4 Stages of acute kidney injury according to each classification

Stages, *n* (%)	KDIGO	AKIN	RIFLE	CK	*P* value
Stage 0	1357 (82.3)	1365 (82.9)	1439 (87.3)	1458 (88.5)	0.967
Stage 1	200 (12.1)	199 (12.1)	118 (7.2)	103 (6.3)	0.370
Stage 2	53 (3.2)	49 (3.0)	57 (3.5)	51 (3.1)	0.998
Stage 3	38 (2.3)	34 (2.1)	34 (2.1)	35 (2.1)	> 0.99

Stage 0 is considered as no-acute kidney injury. Data are shown as *n* (%) or mean ± SD. *P* values < 0.05 were considered statistically significant. KDIGO: Kidney Disease Improving Global Outcomes; AKIN: Acute Kidney Injury Network; RIFLE: Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease; CK: Creatinine kinetics.

Table 5 Overlap of classification systems

KDIGO definition	Compared criteria	AKI Stage by RIFLE, AKIN, or CK			
		Stage 0, *n* (%)	R/Stage1, *n* (%)	I/Stage 2, *n* (%)	F/Stage 3, *n* (%)
Stage 0	RIFLE	1348 (99.3)	9 (0.1)	0	0
Stage 1		126 (63.0)	72 (36.0)	2 (1.0)	0
Stage 2		31 (58.5)	2 (3.8)	19 (35.9)	1 (1.9)
Stage 3		14 (36.8)	2 (5.3)	4 (10.5)	18 (47.4)
Stage 0	AKIN	1344 (99.1)	12 (0.9)	0	0
Stage 1		17 (8.5)	183 (91.5)	0	0
Stage 2		2 (3.8)	3 (5.7)	48 (90.6)	0
Stage 3		2 (5.3)	1 (2.6)	1 (2.6)	34 (89.5)
Stage 0	CK	1346 (99.3)	5 (0.4)	2 (0.2)	3 (0.2)
Stage 1		66 (33.0)	89 (44.5)	40 (20.0)	5 (2.5)
Stage 2		31 (58.5)	3 (5.7)	6 (11.3)	13 (24.5)
Stage 3		15 (39.5)	6 (15.8)	3 (7.9)	14 (36.8)

Stage 0 is considered no Acute Kidney Injury. Stage 1 is at risk. Stage 2 is injury. Stage 3 is failure. KDIGO: Kidney Disease Improving Global Outcomes; AKIN: Acute Kidney Injury Network; RIFLE: Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease; CK: Creatinine kinetics.

RESULTS

Characteristics of the patients

From the 2862 patients retrieved from the MIMCS-III database, 1214 were excluded (536 for being discharged within 24 h, 39 for being < 18 years of age, 529 with missing data, and 110 for being with ESRD), and 1648 were examined for the presence of AKI. Of those patients with TBI, 291 (17.7%) had AKI according to the KDIGO criteria (Figure 1). After PSM, the mean age of the patient cohort was 55.3 ± 23.9 years. Patients with AKI had higher SAPS II (36.6 ± 15.9 *vs* 33.1 ± 13.4, $P = 0.004$) and SOFA (4.8 ± 3.1 *vs* 4.0 ± 2.7, $P = 0.001$) scores, compared with patients without AKI. Moreover, patients with AKI had a higher frequency of shock (35.7% *vs* 25.1%, $P = 0.007$) and had more transfusions of red blood cells (RBC) (377.3 ± 1433.2 *vs* 174.1 ± 623.1 mL, $P = 0.027$) (Table 1). Table 2 shows the characteristics of the study population before PSM.

The patients with AKI were divided according to KDIGO stage 1 ($n = 200$), 2 ($n = 53$), and 3 ($n = 38$) (Table 3). The patients with KDIGO stage 2 were older than in the two other groups ($P = 0.001$) and had a higher proportion of females ($P < 0.001$). The Elixhauser score, SAPS II, and SOFA scores were higher in the stage 3 group compared with the two other groups (all $P < 0.001$). The proportion of shock was higher in stage 3 ($P = 0.004$), the use of vancomycin was higher in stage 1 ($P < 0.001$), the use of aminoglycosides was higher in stages 2 and 3 ($P = 0.040$), and transfusions were higher in stage 3 patients (all $P \leq 0.01$).

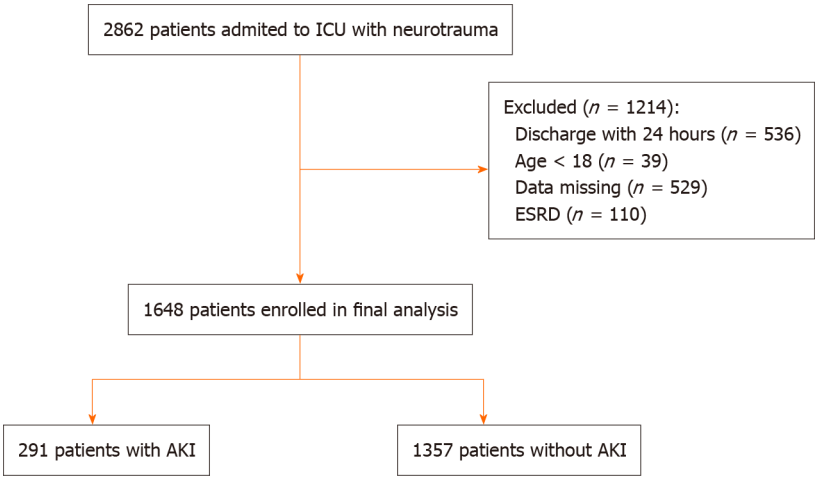

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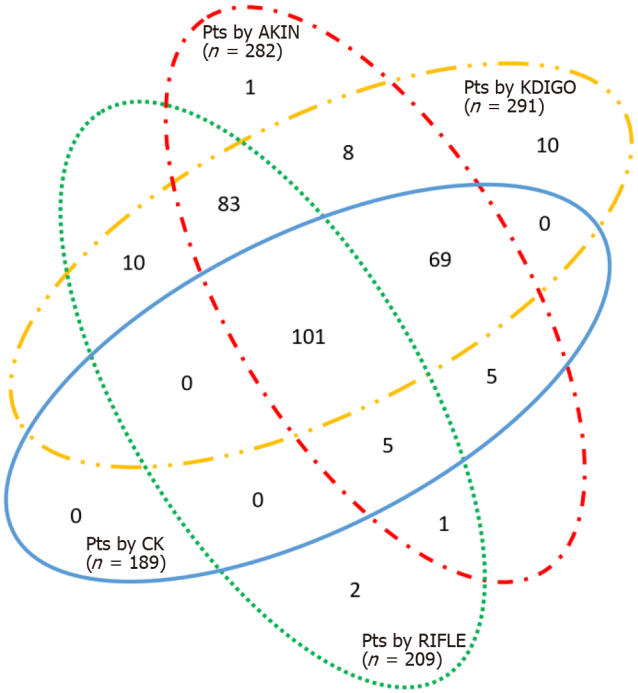
Figure 1 Flow chart of the study. ICU: Intensive care unit; ESRD: End-stage renal disease; AKI: Acute Kidney Injury.



	# Patients	% Mortality	# LOS
ALL FOUR	101	31.68%	8.02
RIFIE ONLY	2	50.00%	9.00
AKIN ONLY	1	100.00%	5.00
KDIGO ONLY	10	10.00%	7.18
CK ONLY	0	N/A	N/A
RIFIE and AKIN only	1	100.00%	2.00
RIFIE and KDIGO only	10	30.00%	9.90
RIFIE and CK only	0	N/A	N/A
AKIN and KDIGO only	8	12.50%	12.88
AKIN and CK only	5	20.00%	1.40
KDIGO and CK only	0	N/A	N/A
Not by RIFLE	69	18.84%	5.65
Not by CK	83	22.89%	3.36
Not by AKIN	0	N/A	N/A
Not by KDIGO	5	20.00%	2.60

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Figure 2 Definition overlap and in-hospital mortality of patients diagnosed by Creatinine kinetics, "Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease", Acute Kidney Injury Network, and Kidney Disease Improving Global Outcomes. Each number in the figure represents the number of patients correctly identified with acute kidney injury by the different definitions represented by the colored circles. For example, 101 patients are included in all four circles, meaning that they have been correctly classified by all four definitions, while 83 patients were correctly identified by "Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease" (RIFLE), Acute Kidney Injury Network (AKIN), and Kidney Disease Improving Global Outcomes (KDIGO). KDIGO was shown in yellow; AKIN in red; RIFLE in green; and Creatinine kinetics in blue. LOS: Length of stay (day); CK: Creatinine kinetics; RIFLE: Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease; AKIN: Acute Kidney Injury Network; KDIGO: Kidney Disease Improving Global Outcomes.

Inter-definition agreement

The incidence of AKI and stages determined by each classification method were examined. The highest incidence of AKI was found by KDIGO (17.7%), followed by AKIN (17.1%), RIFLE (12.7%), and CK (11.5%). There were no differences in the incidence of AKI among the four definitions (P = 0.967) (Table 4).

The identification of AKI overlaps across all the definitions (Figure 2). KDIGO identified the most AKI patients, and CK identified the least. Ten patients were identified as AKI only by KDIGO, while two and one were identified only by RIFLE and AKIN, respectively. KDIGO and AKIN failed to identify 14 and 22 AKI patients, respectively, while CK failed to identify 115 cases. For patients identified by

Table 6 Prognosis-related indicators in patients

Indicators	Non-AKI	AKI			*P* value
	Stage 0 *n* = 291	Stage 1 *n* = 200	Stage 2 *n* = 53	Stage 3 *n* = 38	
Ventilation (h)	105.5 ± 132.4	135.4 ± 149.8	138.7 ± 206.7	149.1 ± 207.1	0.029
ICU duration (d)	4.7 ± 5.8	6.5 ± 7.4	5.6 ± 9.1	6.3 ± 9.2	0.001
Hospitalization (d)	10.8 ± 11.0	13.9 ± 14.6	12.6 ± 13.1	12.4 ± 10.2	0.008
Hospital mortality	185 (12.9)	38 (19.0)	14 (26.4)	17 (44.7)	0.001
30-d mortality	202 (14.9)	42 (21.0)	14 (26.4)	17 (44.7)	< 0.001
1-yr mortality	316 (23.3)	51 (25.5)	17 (32.1)	21 (55.3)	< 0.001

Data are shown as *n* (%) or mean ± SD. *P* values < 0.05 were considered statistically significant. Acute kidney injury and its stage were diagnosed by the Kidney Disease Improving Global Outcomes criteria. AKI: Acute kidney injury; ICU: Intensive care unit.

Table 7 Association between in-hospital mortality and the acute kidney injury stages in diagnosed by Creatinine kinetics, "Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease", Acute Kidney Injury Network, and Kidney Disease Improving Global Outcomes

Variables		Univariable analysis		Multivariable analysis	
		Odds ratio (95%CI)	*P* value	Odds ratio (95%CI)	*P* value
KDIGO	Stage 1	1.64 (1.11-2.41)	0.013	0.70 (0.27-1.83)	0.635
	Stage 2	2.51 (1.33-4.71)	0.004	0.15 (0.00-4.76)	0.242
	Stage 3	5.65 (2.92-10.93)	< 0.001	0.10 (0.00-7.83)	0.705
RIFLE	Stage 1	1.86 (1.16, 2.96)	0.010	0.97 (0.39-2.43)	0.879
	Stage 2	2.70 (1.48-4.90)	0.001	3.26 (0.18-59.43)	0.166
	Stage 3	6.14 (3.08-12.25)	< 0.001	1.90 (0.07-49.94)	0.466
AKIN	Stage 1	1.77 (1.21-2.59)	0.004	1.32 (0.39-4.40)	0.933
	Stage 2	2.54 (1.32-4.88)	0.005	3.23 (0.33-31.98)	0.552
	Stage 3	6.25 (3.13-12.49)	< 0.001	16.88 (0.74-349.18)	0.403
CK	Stage 1	1.49 (0.89-2.51)	0.132	1.34 (0.44-4.83)	0.500
	Stage 2	2.49 (1.32-4.70)	0.005	1.07 (0.35-3.25)	0.579
	Stage 3	4.40 (2.20-8.79)	< 0.001	0.72 (0.17-2.98)	0.615

ORs are adjusted for ethnicity, age, sex, Elixhauser score, simplified acute physiology score, SOFA, Glasgow Coma Scale, craniotomy, max creatinine, creatinine at admission, use of antiplatelet drugs, anticoagulant, vancomycin, angiotensin receptor blocker/angiotensin-converting enzyme inhibitor and aminoglycosides, transfusion, red blood cell, plasma and shock. P values < 0.05 were considered statistically significant. KDIGO: Kidney Disease Improving Global Outcomes; AKIN: Acute Kidney Injury Network; RIFLE: Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease; CK: Creatinine kinetics; CI: Confidence interval.

AKIN and KDIGO only, the patients' length of stay was the longest among all other combinations (12.9 d).

The concordance of AKI diagnosis and staging were further evaluated between KDIGO and the other classifications, using KDIGO as the diagnostic standard (Table 5). Compared with KDIGO, RIFLE correctly staged 1348/1357 (99.3%) stage 0 patients, 72/200 (36.0%) stage 1 patients, 19/53 (35.9%) stage 2 patients, and 18/38 (47.4%) stage 3 patients. Compared with KDIGO, AKIN correctly staged 1344/1357 (99.1%) stage 0 patients, 183/200 (91.5%) stage 1 patients, 48/53 (90.6%) stage 2 patients, and 34/38 (89.5%) stage 3 patients. Compared with KDIGO, CK correctly staged 1346/1357 (99.3%) stage 0 patients, 89/200 (44.5%) stage 1 patients, 6/53 (11.3%) stage 2 patients, and 14/38 (36.8%) stage 3 patients. Concordance was 88.4% between KDIGO and RIFLE, 97.6% between KDIGO and AKIN, and 88.3% between KDIGO and CK.

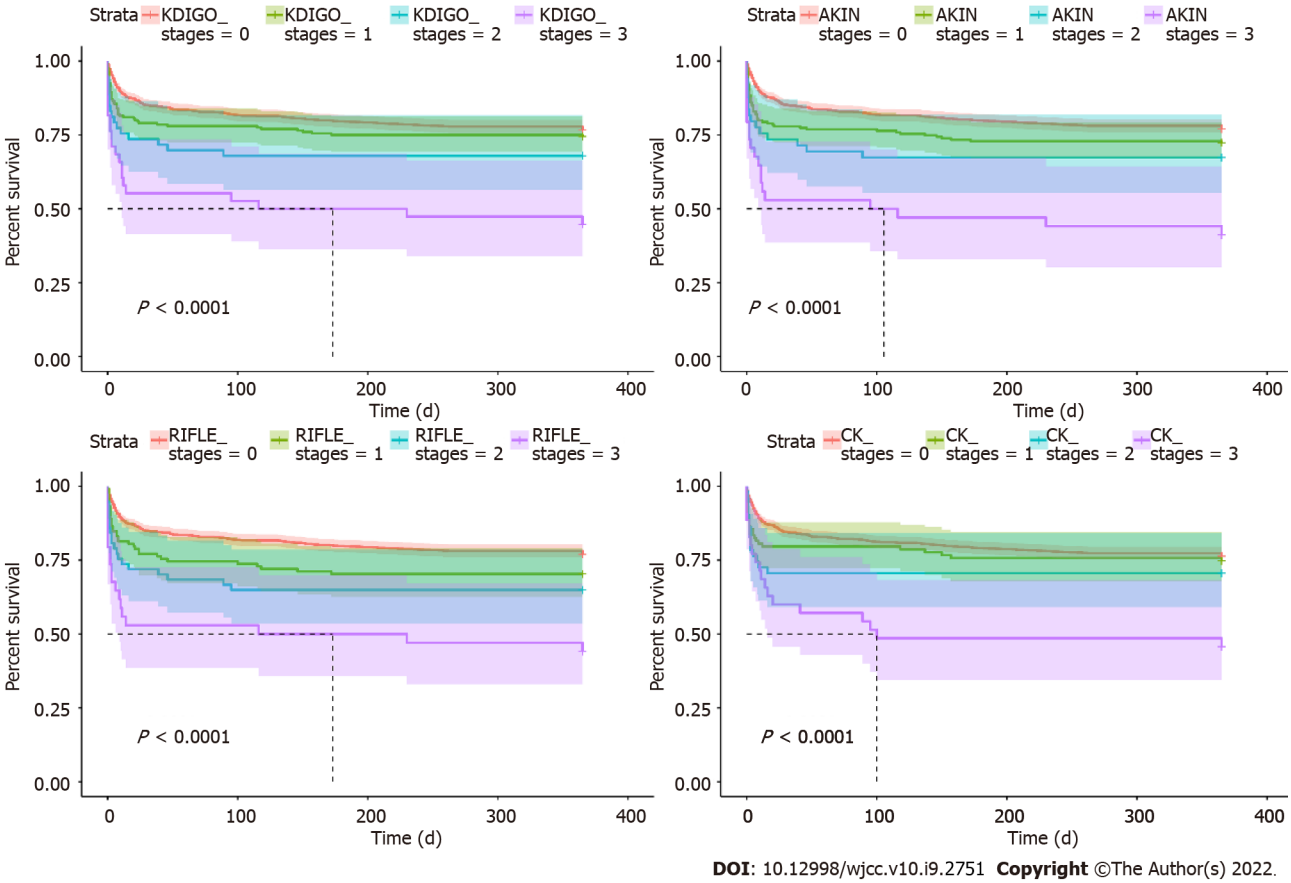

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Figure 3 In-hospital mortality of patients diagnosed by Creatinine kinetics, "Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease", Acute Kidney Injury Network, and Kidney Disease Improving Global Outcomes. CK: Creatinine kinetics; RIFLE: Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease; AKIN: Acute Kidney Injury Network; KDIGO: Kidney Disease Improving Global Outcomes. *P* values < 0.05 were considered statistically significant.

Prognosis

Regardless of AKI determination criteria, the in-hospital mortality was higher for those with AKI than those without. Moreover, the in-hospital mortality increased with the AKI stage (all $P < 0.001$) (Figures 3 and 4).

When staged according to KDIGO, ventilation time increased with AKI stage ($P = 0.03$), and ICU stay and hospitalization were longer for any-stage AKI compared to non-AKI (all $P < 0.05$). In-hospital mortality ($P = 0.001$), 30-d mortality ($P < 0.001$), and 1-year mortality ($P < 0.001$) increased with the AKI stage (Table 6).

The association between severity of AKI by all definitions/stages and in-hospital mortality was tested. As shown in Table 7, the severity of AKI by all definitions and stages was associated with in-hospital mortality in the univariable analyses (all $P < 0.05$), except for stage 1 by CK ($P > 0.05$), but the associations were no longer significant in the multivariable analyses (all $P > 0.05$).

DISCUSSION

For the diagnosis and staging of AKI, at least four different AKI criteria, RIFLE, AKIN, CK, and KDIGO, have been proposed. However, the power of these criteria among TBI patients needs further exploration. This study revealed that differences were seen in AKI diagnosis among the four AKI criteria. The highest incidence of AKI was found by KDIGO (17.7%), followed by AKIN (17.1%), RIFLE (12.7%), and CK (11.5%). Concordance to KDIGO was the lowest for CK, followed by RIFLE and AKIN. The in-hospital mortality rates increased with the AKI stage in all four definitions, but the severity of AKI by all definitions and stages was not associated with in-hospital mortality in the multivariable analyses.

The diagnosis of AKI in patients with TBI has significant clinical relevance, given the requirements for prompt medical intervention for AKI patients. Similar to the results of a previous study[23], this study suggested that the incidence of AKI varied depending on the criteria used, which may lead to confusion during criteria selection and may negatively affect the efficiency of clinical treatment. Some

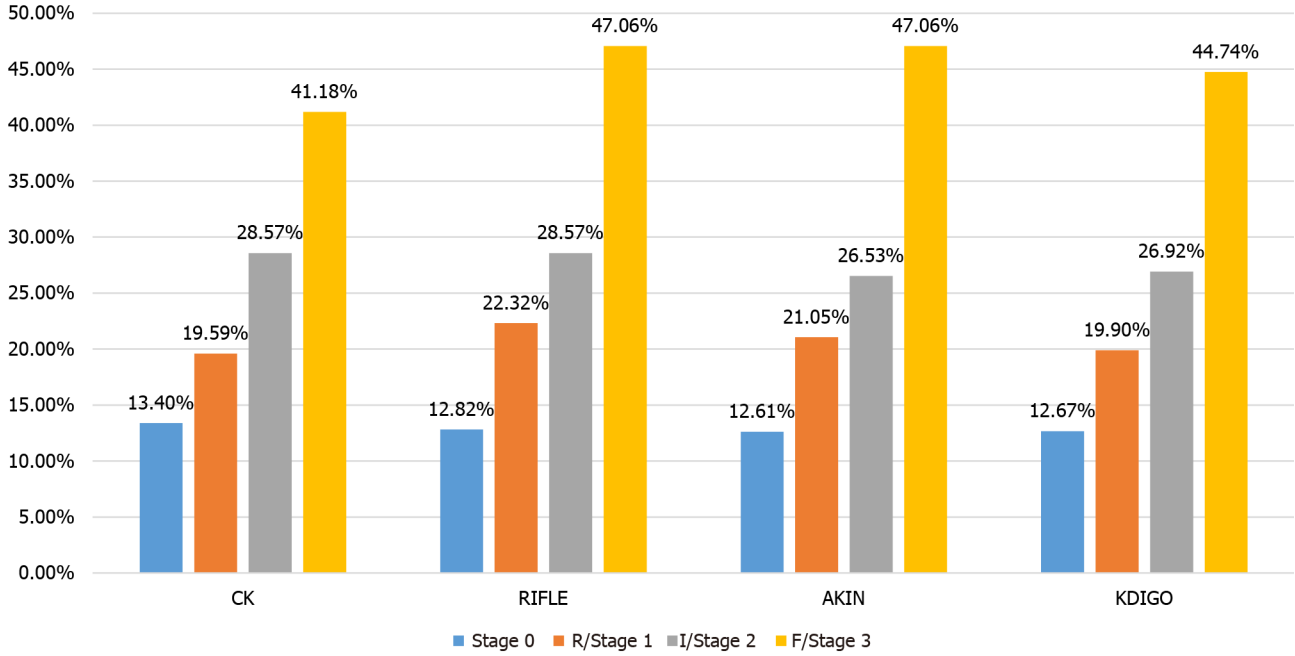

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Figure 4 Percentage of in-hospital mortality for each stage of Acute kidney injury diagnosed by Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease, Acute kidney injury network, Creatinine kinetics, and Kidney Disease Improving Global Outcomes. Stage 0 is considered no AKI. Stage 1 is at risk. Stage 2 is injury. Stage 3 is failure. AKI: Acute Kidney Injury; KDIGO: Kidney Disease Improving Global Outcomes; AKIN: Acute Kidney Injury Network; RIFLE: Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease; CK: Creatinine kinetics.

studies showed that KDIGO is more sensitive than AKIN and RIFLE in AKI diagnosis in patients with myocardial infarction and acute decompensated heart failure[9,10]. In a study comparing KDIGO and CK in diagnosing AKI in trauma patients, KDIGO was shown to be more sensitive, and CK was found to be superior to KDIGO only in patients with pre-existing chronic kidney disease (CKD)[7]. In the present study, the KDIGO classification identified the highest incidence of AKI and was more able to detect than RIFLE, CK, and AKIN. Although there were no significant differences in the proportions of patients with AKI according to the different criteria, misclassification was observed, particularly with the CK and RIFLE definitions.

More specifically, the present study showed the highest incidence of AKI was found by KDIGO (17.7%), followed by AKIN (17.1%), RIFLE (12.7%), and CK (11.5%) among patients with TBI patients. The reason for the difference may be the selection of the baseline SCr to be used for evaluating AKI. For example, the AKIN criteria consider the lowest SCr measurement during the ICU stay as the baseline SCr level, and it probably overestimates the AKI incidence, which can be as high as 74.2%-85.0%[24-27]. However, when baseline SCr was estimated using the MDRD equation, AKI incidence was reported to be 11.6%-23% based on the RIFLE or AKIN criteria[7,10]. The selection of baseline SCr could also affect the incidence of AKI in the general population when following the KDIGO criteria. A possible explanation for this finding is the temporary overhydration during hospitalization. The creatinine concentration extrapolated by the MDRD equation (with a GFR of 75 mL/min) might be more accurate, although it should be used with caution. Other influencing factors include, but are not limited to, UO and population heterogeneity, and further studies are needed in the future.

The KDIGO classification was rarely compared to other AKI definitions regarding its prognostic power in TBI patients. According to Tsai *et al*[24], the KDIGO classification has a relatively higher discriminatory power (0.840 ± 0.032) in predicting in-hospital mortality than the RIFLE (0.826 ± 0.033) and AKIN (0.836 ±0.032) classifications. Zeng *et al*[28] showed that the incidence of AKI changed with the definition but that all definitions were associated with in-hospital mortality. In the present study, KDIGO did not improve the predictive performance of in-hospital mortality, *i.e.*, the in-hospital mortality increased with the increasing stage in all four definitions. On the other hand, the associations disappeared for all four definitions in the multivariable regression analyses after adjusting for ethnicity, age, sex, Elixhauser score, SAPS II, SOFA, GCS, craniotomy, max creatinine, creatinine at admission, use of antiplatelet drugs, anticoagulant, vancomycin, ARB/ACE-I and aminoglycosides, transfusion, red blood cell, plasma, and shock. Therefore, the results mean that one or multiple factors included in the adjusted analyses are a stronger predictor of mortality than AKI in patients with TBI. A study by Ulger *et al*[25] showed that the in-hospital mortality for stage 2 and 3 AKI in AKIN, RIFLE, and KDIGO was nearly the same. These discrepancies might be attributable to the baseline creatine estimation based on the MDRD formula[15]. Besides, clinically, death attributable to AKI is rare in TBI patients, which may

explain the lack of association between the four definitions and in-hospital mortality. Osmotic therapy during ICU stay appears to affect the mortality due to AKI[29]. A recent study suggested that the AKI stage was associated with mortality in patients with TBI, but not AKI duration or AKI burden; in addition, most deaths occurred during the first 3 d of ICU stay[30]. The use of renoprotective measures affects the mortality due to AKI in patients with TBI[31].

There are some limitations to this research. First, as a retrospective, a single-center study from a single academic hospital, the generalizability of these findings is questionable. Incidence estimates, mortality rates, and procedures vary greatly among hospitals and countries. Second, baseline creatinine was calculated as a theoretical baseline SCr for a given patient assuming a normal GFR, which may overestimate or underestimate the incidence of AKI to some extent. Third, the patients were identified using the administrative codes entered in the database, which is subject to bias regarding the use of the incorrect code by the physicians and administrative personnel[17].

CONCLUSION

In conclusion, this study indicates that in patients with TBI, differences are seen in AKI diagnosis among the four AKI definitions or stages, and concordance varies, as well as the in-hospital mortality. Thus, more universal AKI criteria are needed in patients with TBI. Besides, the severity of AKI was not associated with in-hospital mortality rates when using any of the four definitions.

ARTICLE HIGHLIGHTS

Research background

Early identification and subsequent clinical intervention of acute kidney injury (AKI) in traumatic brain injury (TBI) patients are critical to survival.

Research motivation

The exact definition of AKI for patients with TBI is unknown.

Research objectives

We aimed to compare four AKI diagnostic criteria to determine AKI incidence/stage and their association with the in-hospital mortality rate of patients with TBI.

Research methods

The subjects in this study were assessed for the presence and stage of AKI using four different AKI diagnostic criteria.

Research results

The in-hospital mortality rates increased with the AKI stage in all four definitions. The severity of AKI by all definitions and stages was not associated with in-hospital mortality in the multivariable analyses (all $P > 0.05$).

Research conclusions

This study revealed that Kidney Disease Improving Global Outcomes (KDIGO) is the best method to define AKI in patients with TBI.

Research perspectives

In the future, it is necessary to increase the sample size for prospective studies to further explore.

FOOTNOTES

Author contributions: Yu XX and Liu Y conceived and coordinated the study, designed, performed and analyzed the experiments, wrote the paper; Wang JX, Tian JF, Zeng WX, Jiang S and Lv RG carried out the data collection and preprocess of the raw data; Huang ZY, Huang HF and Huang SH performed the data analysis; Liu Y and Gao JL revised the paper; all authors reviewed the results and approved the final version of the manuscript.

Institutional review board statement: The study was approved by the Ethics Committee for Human Research of Shenzhen Hospital, Southern Medical University, No. YS2YYEC20180009.

Informed consent statement: Patients were not required to give informed consent to the study because the analysis

used anonymous clinical data that were obtained after each patient agreed to treatment by written consent.

Conflict-of-interest statement: The authors declare that they have no conflict of interest.

Data sharing statement: No additional data are available.

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