

Validation of Renal Risk Score Models for Coronary Artery Bypass Surgery in Diabetic Patients



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Background

Coronary artery bypass grafting is applicable with very low mortality and morbidity rates around the world. However, exposure to even one of the risk factors increases mortality and morbidity significantly. There are three acute kidney injury definitions, and classification methods are applicable (Kidney Disease: Improving Global Outcomes (KDIGO); Risk, Injury, Failure, Loss of kidney function and End-stage kidney disease (RIFLE); and Acute Kidney Injury Network (AKIN)), for understanding and grading of renal impairment. With these definitions, it became possible to take measures at an early stage and start the management process. Methods for assessing renal impairment after coronary artery bypass grafting (CABG) specifically in patients with diabetes mellitus require further investigation. We compared these three acute kidney injury definitions for prediction of outcomes in diabetic patients undergoing coronary artery bypass grafting procedure.

Methods

Between January 2010 and December 2013, a total of 617 consecutive patients with diabetes mellitus undergoing coronary artery bypass grafting (CABG) with cardiopulmonary bypass in our institution were included in the study.

Results

We considered 617 CABG operations on diabetes mellitus patients for this study from January 2010 to December 2013. The three scores provided good discriminative capacity in the global patient sample, with the area under the ROC curve (AUC) being higher, RIFLE (0.803, 95% CI: 0.724–0.882). The goodness of fit was good for all scales.

Conclusions

Especially in on-pump CABG patients with diabetes mellitus, we can use AKIN, RIFLE, and KDIGO scoring systems to predict early diagnosis for acute kidney injury (AKI). In our analysis, the KDIGO criterion was superior to AKIN and RIFLE with regard its prognostic power.

Keywords

Acute kidney failure • Coronary artery bypass • Diabetes mellitus • RIFLE • AKIN • KDIGO

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Introduction

Coronary artery bypass grafting (CABG) is applicable with very low mortality and morbidity rates around the world. However, exposure to even one of the risk factors increases mortality and morbidity significantly [1]. Renal impairment, even with a slight increase in serum creatinine level after cardiac surgery, impacts outcomes [2–5]. Diabetes mellitus is one of the major causes of renal impairment worldwide. The patients are affected in a wide variety of ways from albuminuria to renal replacement therapy. Also, patients with diabetes mellitus (DM) are three to four times more likely to die of ischaemic heart disease than from any other single condition [6]. Diabetic patients are particularly prone to diffuse, multivessel coronary artery disease (CAD) [7], for which current guidelines recommend CABG as the myocardial revascularisation modality of choice [8]. For these reasons, the proportion of patients undergoing CABG who have DM has increased steadily over the last 15 years; diabetic patients now accounting for approximately one quarter of patients undergoing CABG [9,10]. More than 40% of adults with DM have renal impairment (RI) characterised by either albuminuria or reduced glomerular filtration rate [11]. Both DM and RI are predictors of increased mortality following CABG [12–14]. However, despite the common coexistence of these two conditions, there are few data that describe the impact on prognosis after CABG of each factor relative to the other and the two in combination. That is why, during the postoperative period, close follow-up of renal functions is crucial. There are three acute kidney injury definitions, and classification methods are as follows: Kidney Disease: Improving Global Outcomes (KDIGO); Risk, Injury, Failure, Loss of kidney function and End-stage kidney disease (RIFLE); and Acute Kidney Injury Network (AKIN), for understanding and grading of renal impairment [15–17]. With these definitions, it became possible to take measures at an early stage and start the management process.

Methods for assessing renal impairment after CABG specifically in patients with diabetes mellitus require further investigation. We compared these three acute kidney injury definitions for prediction of outcomes in diabetic patients undergoing coronary artery bypass grafting procedure.

Materials and Methods

This study was approved by the institutional review board and written informed consent was obtained from all participants. Between January 2010 and December 2013, a total of 617 consecutive patients with diabetes mellitus undergoing CABG with cardiopulmonary bypass in our institution were included in this study. The diagnosis of diabetes mellitus was confirmed with patients' HbA1c levels. Patients with HbA1c more than 6.5 mg/dl were accepted as diabetic and included in the study [18]. Also, patients under diabetes treatment were included. Oral antidiabetic medications were

Table 1 All patients demographics.

All patients n = 616		
Age (years) mean ± std		60.50 ± 9.17
Women (n) %		(213) 34.5%
Previous MI (n) %		(249) 40.4%
Previous Cardiac Surgery (n) %		(13) 2.1%
HT (n) %		(336) 54.5%
PAD (n) %		(29) 4.7%
COPD (n) %		(82) 13.3%
Use of Calcium Channel Blocker		(66) 10.7%
Use of Insulin (n) %		(144) 23.3%
Preoperative Haemoglobin	preoperative	12.74 ± 1.71
Albumin	preoperative	4.11 ± 0.47
	postoperative	3.23 ± 0.42
HbA1c	preoperative	8.69 ± 1.72
Type of surgery	CABG (mean revascularised artery)	2.58 ± 1.05
	Combined Surgery	59 (9.6%)
CPB (n) %		(544) 88.2%
Time of ECC (h)		88.49 ± 48.96
Time of ACC (h)		54.27 ± 35.94
Mechanic ventilation (hours)		18.56 ± 53.12
ICU stay (hours)		72.30 ± 82.07
Hospital stay (days)		11.26 ± 10.92
Re ICU requirement (n) %		(28) 4.25%
Haemodialysis (n) %		(35) 5.7%
GFR (ml/min)		72.44 ± 49.30
Hospital mortality (n, %)		(23) 3.7%
Proteinuria		(68) 11.0%

Abbreviations: MI, myocardial infarction; HT, hypertension; PAD, peripheral arterial disease; COPD, chronic obstructive pulmonary disease; CABG, coronary artery bypass grafting; CPB, cardiopulmonary bypass; ACC, aortic cross-camp; ICU, intensive care unit; GFR: glomerular filtration rate; ECC.

rearranged to change insulin treatment according to endocrinologist recommendations. Patients with accompanying surgery of coronary artery bypass grafting procedure were excluded. Patients with a history of pre-existing renal replacement therapy and intraoperative haemofiltration were excluded. Also, within the first 7 days, patients who died were excluded since it was not possible to perform the RIFLE criteria. During in-hospital stay, patients were given insulin treatment according to blood glucose level following endocrinologist recommendations.

Table 2 Demographics according to groups.

	AKIN			RIFLE			KDIGO			Renal Replacement Therapy		
	AKIN (-)	AKIN (+)	<i>p</i>	RIFLE (-)	RIFLE (+)	<i>p</i>	KDIGO (-)	KDIGO (+)	<i>p</i>	Dialysis (+)	Dialysis is (-)	<i>p</i>
	n = 422 (68.4%)	n = 195 (31.6%)		n = 476 (77.1%)	n = 141 (22.9%)		n = 402 (65.2%)	n = 215 (34.8%)		n = 35 (5.7%)	n = 582 (94.3%)	
Age (years)	59.98 ± 9.07	61.59 ± 9.33	0.043	59.99 ± 8.95	62.18 ± 9.72	0.013	59.70 ± 9.07	61.96 ± 9.20	0.003	60.36 ± 9.07	62.71 ± 10.68	>0.05
Women (n)	136	77	>0.05	141	72	0.000	125	88	0.014	195	18	0.030
Previous MI (n)	157	92	0.019	187	62	>0.05	151	98	>0.05	234	15	>0.05
Previous cardiac surgery	10	3	>0.05	11	2	>0.05	10	3	>0.05	11	2	>0.05
HT	218	118	0.000	249	87	0.003	209	127	0.001	315	21	>0.05
PAD	23	6	>0.05	25	4	>0.05	23	6	>0.05	26	13	>0.05
COPD	53	29	>0.05	63	19	>0.05	51	31	>0.05	70	12	0.000
Use of calcium channel blocker	37	29	0.023	49	17	>0.05	36	30	>0.05	65	1	>0.05
Use of insulin	101	122	>0.05	172	58	>0.05	148	80	>0.05	216	14	>0.05
Haemoglobin preoperative	12.94 ± 1.68	12.30 ± 1.70	0.000	12.91 ± 1.69	12.17 ± 1.68	0.000	12.99 ± 1.68	12.26 ± 1.68	0.000	12.83 ± 1.69	11.35 ± 1.61	0.000
Albumin preoperative	4.15 ± 0.48	4.01 ± 0.44	0.000	4.15 ± 0.47	3.98 ± 0.46	0.001	4.16 ± 0.48	4.01 ± 0.44	0.000	4.14 ± 0.46	3.65 ± 0.48	0.000
Albumin postoperative	3.25 ± 0.39	3.18 ± 0.47	0.019	3.26 ± 0.44	3.14 ± 0.37	0.006	3.25 ± 0.40	3.18 ± 0.46	>0.05	3.26 ± 0.42	2.93 ± 0.35	0.000
HbA1c preoperative	8.71 ± 1.75	8.65 ± 1.66	>0.05	8.72 ± 1.73	8.59 ± 1.69	>0.05	8.69 ± 1.74	8.68 ± 1.68	>0.05	8.70 ± 1.73	8.45 ± 1.62	>0.05
Type of surgery												
CABG (mean revascularised artery)	2.55 ± 1.03	2.61 ± 1.08	>0.05	2.59 ± 1.04	2.51 ± 1.07	>0.05	2.56 ± 1.03	2.59 ± 1.07	>0.05	2.59 ± 1.05	2.34 ± 0.99	>0.05
Combined surgery	28	31	0.000	34	25	0.000	26	13	0.000	48	11	0.000
CPB	367	177	>0.05	418	126	>0.05	351	149	>0.05	512	32	>0.05
Time of ECC (h)	83.98 ± 46.15	98.87 ± 53.62	0.003	86.85 ± 48.65	94.12 ± 49.80	>0.05	84.01 ± 45.59	97.33 ± 54.08	>0.05	87.46 ± 48.68	107.38 ± 51.24	0.043
Time of ACC (h)	51.61 ± 34.45	60.46 ± 38.59	0.014	52.79 ± 35.21	59.41 ± 38.09	>0.05	51.52 ± 33.98	59.76 ± 39.08	0.027	53.15 ± 35.14	75.88 ± 44.37	0.002
Mechanical ventilation (hours)	14.75 ± 49.07	27.40 ± 60.78	0.011	16.85 ± 56.75	24.52 ± 37.28	>0.05	14.88 ± 50.33	25.83 ± 57.72	0.000	17.19 ± 52.27	45.8 ± 63.05	0.007
ICU stay (hours)	59.10 ± 60.02	103.04 ± 112.87	0.000	61.15 ± 59.47	111.44 ± 126.92	0.000	57.76 ± 55.8	101.13 ± 113.09	0.000	64.97 ± 64.71	218.88 ± 190.85	0.000
Hospital stay (days)	10.00 ± 9.15	13.98 ± 13.6	0.000	10.06 ± 8.55	15.33 ± 16.01	0.000	9.55 ± 7.91	14.46 ± 14.51	0.000	10.63 ± 9.87	22.05 ± 19.51	0.000
Re ICU requirement	18	10	>0.05	19	9	>0.05	16	12	>0.05	22	6	0.000
Haemodialysis (n, %)	7	28	0.000	7	28	0.000	5	30	0.000	582	35	na
GFR (ml/min)	88.65 ± 17.83	76.83 ± 4.83	>0.05	88.22 ± 15.82	73.77 ± 6.81	>0.05	89.76 ± 18.71	75.86 ± 4.51	>0.05	71.37 ± 19.91	38.37 ± 14.41	0.000
Hospital mortality (n, %)	8	15	0.000	8	15	0.000	6	17	0.000	8	15	0.000
Proteinuria	41	27	0.029	48	20	>0.05	38	30	0.021	57	11	0.000

Abbreviations: MI, myocardial infarction; HT, hypertension; PAD, peripheral arterial disease; COPD, chronic obstructive pulmonary disease; CABG, coronary artery bypass grafting; CPB, cardiopulmonary bypass; ACC, aortic cross clamp; ICU, intensive care unit; GFR, glomerular filtration rate.

Serum Creatinine Measurements

Serial measurements of serum creatinine values were analysed for every day of admission from baseline admission date until discharge. All creatinine assays were carried out in a single laboratory.

Glomerular filtration rate was assessed by the Cockcroft-Gault equation [19].

Definitions

KDIGO: Increase in serum creatinine equal to or greater than 0.3 mg/dL in 48 hours, or equal to or greater than 1.5 times the baseline creatinine for up to 7 days [15].

RIFLE: Increase in serum creatinine equal to or greater than 1.5 mg/dL above baseline creatinine for up to 7 days [16].

AKIN: Increase in serum creatinine equal to or greater than 0.3 mg/dL, or equal to or greater than 1.5 times the baseline creatinine level at a 48-hour moving window [17].

Statistical Methods

Continuous variables were displayed by mean and standard deviation if normally distributed and by the median and range if there was no normal distribution. Group comparison was made using the unpaired *t*-test or the Mann-Whitney *U*-test in the case of ordinal data or no normal distribution.

Categorical variables were displayed as counts and percentages. Group comparison was done using the χ^2 test or the Fisher's exact test where appropriate. Survival analyses were performed by the Kaplan-Meier survival curves. All tests were two-sided, and a *p*-value of 0.05 or lower was considered statistically significant. All statistical analyses

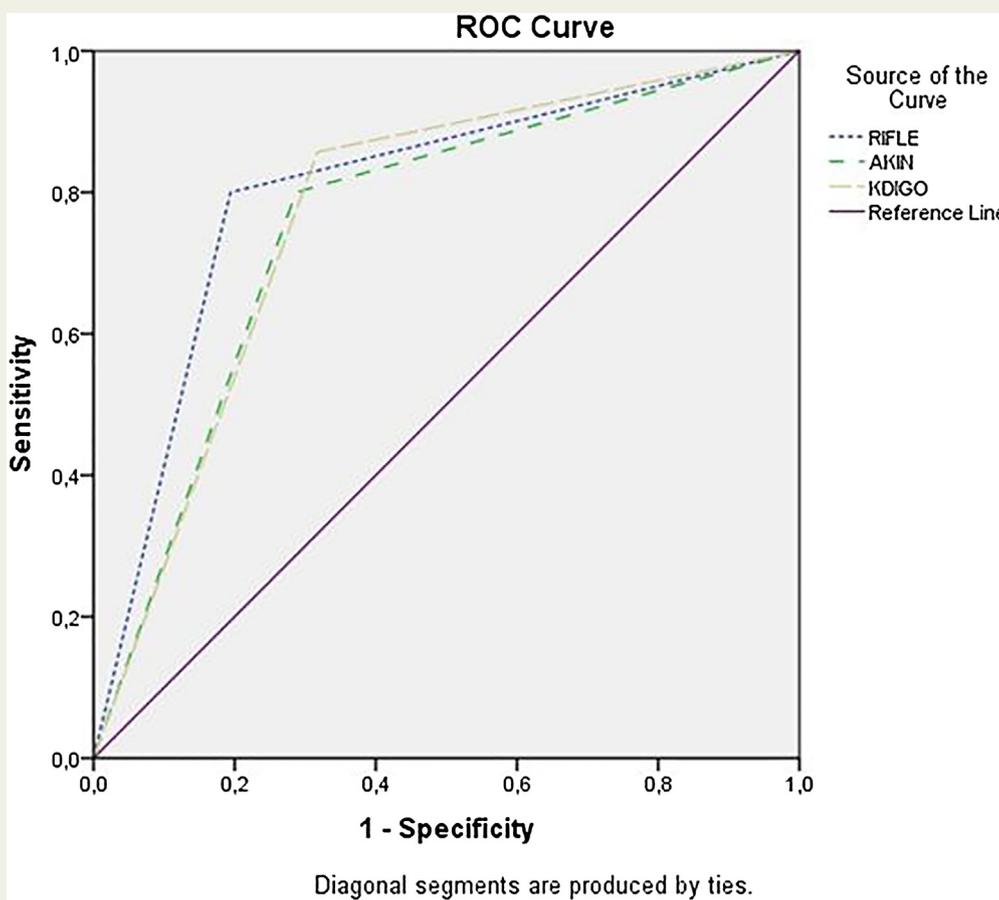


Figure 1 Discriminative Capacity of Risk Scoring Systems.

Discriminative Capacity of Risk Scoring Systems				
Classification	Area (AUC)	<i>p</i>	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
AKIN	0.757	0.000	0.677	0.836
KDIGO	0.770	0.000	0.697	0.842
RIFLE	0.803	0.000	0.724	0.882

Table 3 Hosmer and Lemeshow Test.

	Chi-square	df	Sig.
AKIN	8.869	8	0.354
KDIGO	5.674	8	0.684
RIFLE	4.630	8	0.796

Abbreviations: KDIGO, Kidney Disease: Improving Global Outcomes; RIFLE, Risk, Injury, and Failure, Loss, and End-stage kidney disease; AKIN, Acute Kidney Injury Network.

were performed using IBM-SPSS 21 (IBM Corp. Released 2012, IBM SPSS Statistics for Windows, Version 21.0, IBM Corp. Armonk, NY, USA).

Results

We considered 617 CABG operations on diabetes mellitus patients for this study from January 2010 to December 2013. The mean (standard deviation; SD) age of the patients was 60.50 ±9.17 (range: 31–84) years; 213 (34.5%) of them were female. We have shown demographic, perioperative clinical and procedural as well as postoperative follow-up data in [Table 1](#). [Table 2](#) depicts cross tabulation of patients classified by RIFLE, AKIN and KDIGO criteria. The three scores showed good discriminative capacity in the global patient sample, with the area under the ROC curve (AUC) being higher RIFLE (0.803, 95% CI: 0.724–0.882) ([Figure 1](#)). The goodness of fit was good for all scales ([Table 3](#)). Benchmarking of our institutional postoperative renal replacement therapy requirement

rates revealed worse prediction upon KDIGO scoring compared to RIFLE and AKIN ([Figure 2](#)). In follow-up, 35 patients needed haemodialysis. KDIGO predicted the need for haemodialysis in 30 of these 35 patients whereas RIFLE and AKIN predicted 28 out of these 35 patients ([Table 1](#)).

Discussion

Acute kidney injury is a common complication in on-pump coronary artery bypass graft surgery. Renal hypoperfusion, reperfusion, and inflammation may be the reasons for this complication [19]. AKI may have a negative impact on survival in patients undergoing CABG. Furthermore, AKI increases costs and length of hospital stay. Also, renal severity score (RSS) was used to define renal failure in the early stage. As a result, RSS may help renal protection [20]. The incidence of acute renal failure requiring dialysis after CPB is remarkably low, averaging 1%; however, the incidence increases to 5% with complex operations [21]. Some degree of renal injury is inevitable during CPB, and postperfusion proteinuria occurs in all patients [22,23]. After on-pump CABG, 1–30% of patients need haemodialysis [24]. On the other hand, Sampaio reported a range between 15–51% according to criteria they chose [25].

Today, we often use serum creatinine level to diagnose the AKI. Also, creatinine concentrations may not change until 50% of kidney function has already been lost. That is why creatinine may not show renal failure in the early stages [19]. Although there are many studies on new biochemical markers in addition to creatinine, there is still a need for an ideal biochemical marker. In the study

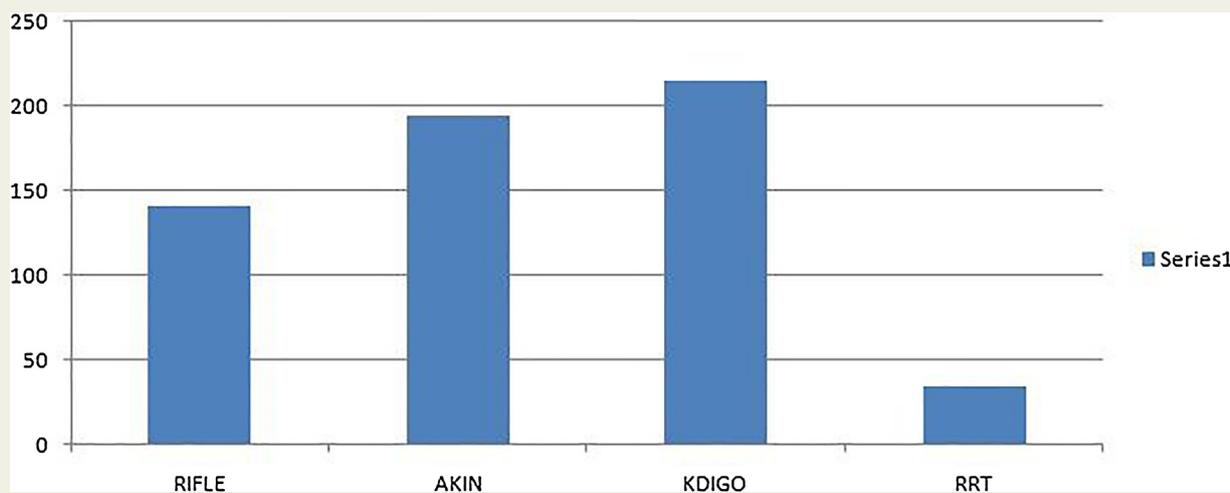


Figure 2 RRT Requirement Prediction.

	RRT Requirement Prediction			Actual RRT Required Patients
	RIFLE	AKIN	KDIGO	RRT
number of patients	141	195	215	35

Abbreviations: RRT, Renal replacement therapy; KDIGO, Kidney Disease: Improving Global Outcomes; RIFLE, Risk, Injury, and Failure, Loss, and End-stage kidney disease; AKIN, Acute Kidney Injury Network.

conducted by Haase, urine and serum neutrophil gelatinase, associated lipocalin levels may be used in on-pump CABG patients for early diagnosis of AKI [26]. RIFLE, AKIN and KDIGO criteria have been created for this purpose. All of these systems use serum creatinine and urine output [15,27,28]. Therefore, we used customised values with various classifications systems to define the AKI. Even with the use of the same criteria, AKI incidence ranged differently. AKIN ranged between 26%, 49–51% [25,29,30] and in our study, we have observed 31.6%. For KDIGO it is reported as 15% and 19% [25,31]. Moreover, in our study KDIGO described 34.8% of patients. RIFLE criteria showed 19%, 30% and 15% [25,30,32] but we have observed 22.9%. Our results are parallel to the literature, but KDIGO described more AKI patients than the literature. Renal risk score systems are invented for usage of the same criteria in the literature and also by way of these new models.

Lopez-Delgado et al. studied the prognostic value of RIFLE classification on the outcomes of patients undergoing cardiac surgery and reported the worst outcome with the RIFLE failure group 22.3% ($p < 0.05$) [33]. In our study, we have observed a better outcome with 53.6% in RIFLE failure group ($p = 0.001$). Machado et al. investigated KDIGO and reported overall the 30-day mortality was 7.1% (2.2%) for patients without AKI and 8.2%, 31% and 55% for patients with AKI at stages 1, 2 and 3, respectively [34]. We have observed 7.9%. Yan et al. reported 78% hospital mortality in patients with stage 3 AKIN renal failure [35]. We have observed 20%.

Comparing all three models showed AUC well. But best AUC was in RIFLE (0.803, 95% CI: 0.724–0.882) model.

Limitations

This study had some limitations. Because this study was retrospective and randomisation was not performed, it is conceivable that there are differences in patient characteristics. Also, the study was held in a multi surgeon-single centre with a relatively reduced number of patients. Additionally, the diagnosis of AKI was based on plasma creatinine level regardless of urinary output.

Conclusion

There are many studies on new biochemical markers to use for early diagnosis of AKI. However, the ideal marker still has not been found; for this reason, there is still a need for comprehensive studies. Especially in on-pump CABG patients with diabetes mellitus, we can use AKIN, RIFLE, and KDIGO scoring systems to predict early diagnosis for AKI. In our analysis, the KDIGO criterion was superior to AKIN and RIFLES with regard to prognostic power.

Conflict of Interest

None declared.

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