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Original Article

The RIFLE Classification: A Stratification Scheme for Patients of Acute Renal Failure after Coronary Artery Bypass Surgery

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Key Words :
IHD, CABG, Renal failure, RIFLE classification.

Abstract

Background: *Acute renal failure is linked to an increased risk of death and morbidity after cardiac surgery. Because there are no standard criteria for acute renal damage, there is a wide variation in the reports that have been published. The Acute Dialysis Quality Initiative Workgroup has developed new RIFLE criteria for acute renal dysfunction. The goal of current study was to appraise whether this definition of postoperative renal dysfunction after coronary artery bypass surgery (CABG) was accurate.*

Methods: *Fifty patients with critical coronary artery disease & undergoing CABG were enrolled in the study. Out of 50 patients, 25 patients had CABG with cardiopulmonary bypass (CPB) and remaining 25 underwent off pump CABG (OPCAB). Patients were distributed into various groups (based on the severity of renal impairment) using the RIFLE classification: Risk, Injury, Failure, Loss, End-stage kidney disease) depending on either serum creatinine level/ estimated glomerular filtration rate (eGFR) or urine output. The variation with 30 days-mortality, ICU stay and renal replacement therapy after CABG were identified.*

Results: *After CABG, 10% of patients experienced renal impairment, as per definitions of RIFLE classification. In this study, there is no significant difference in ARF (RIFLE classification-normal and risk) with or without use of CPB. However, incidence of RIFLE- injury and failure is higher in CPB group than no CPB group. The postoperative proportions of death and renal failure necessitating renal replacement therapy (RRT) were 2% (number of patients, 1 of 50) and 2% (1 of 50), respectively in RIFLE-failure. For the whole study cohort, the median duration of postoperative ICU stay was 4.0 days, with interquartile ranges of 3.0 to 7.0 days. All the patients of Rifle classification-injury and failure had prolonged ICU stay (5 or more days).*

Conclusions: *The RIFLE criteria are a useful tool for determining renal impairment after CABG. Increased renal replacement treatment, longer ICU stays, and a higher death rate are all linked to the severity of RIFLE classification.*

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Introduction:

Postoperative renal insufficiency occurs in 5% to 30% of all cardiac surgical patients and renal failure requiring dialysis occurs in approximately 1 to 5 % of all patients.[1] However, the frequency of acute renal failure (ARF) varies according to type of cardiac surgery. Combination CABG with valve surgery has the highest risk, followed by isolated valvular surgery, while CABG has the lowest risk.[2] Postoperative renal injury is associated with complex and longer hospital stay, a higher risk of infections and high mortality rates, which averages 15 to 30%, but can be as high as 60%. In all documented trials, mortality in ARF that needs dialysis (ARF-D) is steadily high, averaging 60 to 70%.[1] Despite improvement in bypass practices, perioperative intensive care, and hemodialysis strategies, mortality and morbidity linked to ARF have remained consistently high in the last decade. With an odds ratio of 7.9 (95% CI: 6 to 10), the

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ARF in cardiac surgery postoperative patients has been recognized as the most vulnerable factor for mortality.[3] ARF is triggered by various pathways, including hemodynamic, inflammatory, and nephrotoxic causes.[3]

The prevalence of ARF varied based on the research population, comorbidities, operation type, and, in particular, postoperative renal failure criteria. ARF can be defined in a variety of ways, ranging from minor increases in serum creatinine or a decrease in estimated glomerular filtration rate (GFR) to a severe form of the illness requiring dialysis. The RIFLE classification, a new evidence-based consensus criterion for ARF, was established by the Acute Dialysis Quality Initiative (ADQI) Working Group in order to enhance the approach to ARF. The classification elucidates three grades of ARF severity (Risk, Injury and Failure) based on variations in serum creatinine/eGFR and urine output and two clinical outcomes (Loss and End-stage).[4] The RIFLE criteria have been analyzed in numerous clinical investigations involving critically sick ICU patients with ARF to determine its reliability, clinical application, and capacity to predict death.[5] However, these analyses are restricted by the fact that they only studied particular subset of critically ill individuals. As a result, we investigated this categorization of ARF in postoperative CABG patients in the current study.

Methods:

We designed a cohort study in department of Cardiovascular Surgery, Combined military hospital (CMH), Dhaka. Purposive sampling was done, where fifty patients with critical coronary artery disease & recieving CABG from July 2019 to December 2019 were enrolled in the study. Out of 50 patients, 25 patients had history of CABG using CPB and rest 25 patients underwent off pump CABG (OPCAB). Patients with poor LV systolic function (EF <30%), requiring inotropes or intraaortic balloon pump (IABP) preoperatively, emergency & re-do CABG, having other operations performed simultaneously with CABG and patients requiring hemodialysis before surgery were excluded from the analysis.

Patient information included demographics, laboratory results, and hospital outcomes. The computerized hospital records and database were used to retrieve demographic and laboratory data. Urine output was measured every hour, and serum creatinine levels were checked at least once a day. The change in plasma creatinine level was calculated using the difference between the preoperative and maximal concentrations during the course of the ICU stay. The Modification of Diet in Renal Disease equation (MDRD) was used to compute preoperative eGFR and the lowest eGFR during ICU stay.

For women, the product of this equation was multiplied by correction factor of 0.742.[6] The hospital admission creatinine was utilized as a baseline for individuals with a history of renal dysfunction (but not on regular RRT). The outcome variables: the 30-day mortality, the longer (5 or more days) ICU stay and postoperative RRT (intermittent hemodialysis) were recorded. No other major morbidity was evaluated.

The Acute Dialysis Quality Initiative Workgroup designed the categorization system for ARF, which has been titled as RIFLE based on the degree of renal dysfunction (Table I).[4] According to GFR, plasma creatinine (where change from the patient's individual baseline was measured), and urine output, patients were categorized into three severity levels: risk, injury, and failure. Patients receiving renal replacement therapy (RRT) for renal reasons, were considered to have ARF irrespective of their plasma creatinine level or urine output. RIFLE-Normal level refers to patients without renal impairment. In this analysis, the RIFLE outcome classes (loss and end-stage renal disease criteria) were excluded.[4]

The central tendency for continuous data is expressed as the mean ± standard deviation or the median (interquartile range). We tested continuous variables for normality by distribution plots. We compared means using the Student's t test when normally distributed, and the Mann-Whitney U test/Kruskal Wallis when not. The Mann-Whitney U test were performed to evaluate differences between survivors and dead patients and to find differences among RIFLE classification. Comparisons of categorical variables across multiple groups were performed using chi square and *Fisher's exact test*. The SPSS 25 software

Table-I

The RIFLE Classification Scheme for Acute Renal Failure.[4]

	GFR criteria	Urine output criteria
Risk	Increased plasma creatinine x 1.5 or GFR decrease >25%	<0.5 ml. Kg^{-1} . h^{-1} x 6 hours
Injury	Increased plasma creatinine x 2 or GFR decrease >50%	<0.5 ml. Kg^{-1}. h^{-1} x 12 hours
Failure	Increased plasma creatinine x 3 or acute plasma creatinine ≥350 µmol/L or acute rise ≥44 µmol/L	<0.3 ml. Kg^{-1}. h^{-1} x 24 hours or anuria x 12 hours
Loss	Persistent acute renal failure-complete loss kidney function> 4 weeks	
ESKD	End stage kidney disease > 3 months	

(SPSS, Chicago, Illinois) was used in all analyses. For statistics, *p* value less than 0.05 was considered significant.

Results:

Fifty patients underwent CABG throughout the study period. Within this population, 25 patients (50%) had CABG with CPB, while remaining 25 (50%) underwent OPCAB.

Table II: shows comparison of demographic and investigation variables between CPB and no CPB group. There is no significant difference between the groups. Number of patients and percentage or mean ± standard deviation is presented. The *p* values are determined with student's t test/x^2 test.

In this study, there is no significant difference in ARF (RIFLE classification-normal and risk) with

Table-II

Comparison of demographic and investigation variables between CPB and no CPB group.

Independent variables	With CPB	Without CPB	*p* value
Age	56.16±8.6	53.64±6.6	0.250
Sex (Male)	15 (48.4%)	16 (51.6%)	0.50
DM	14 (46.7%)	16 (53.3%)	0.387
HTN	14(50.0%)	14(50.0%)	0.617
CAG			
TVCAD	17(51.5%)	16(48.5%)	0.50
DVCAD	8 (47.1%)	9 (52.9%)	
Ejection fraction	51.76 ± 9.25	51.80	0.988
Serum creatinine			
Preoperative	0.9480±0.16	0.9480 ± 0.144	0.368
Postoperative	1.5120 ±1.26	1.3720 ± 0.672	0.295
eGFR			
Preoperative	82.69±17.23	80.45 ± 15.36	0.360
Postoperative	61.31±20.58	59.70 ± 21.27	0.243

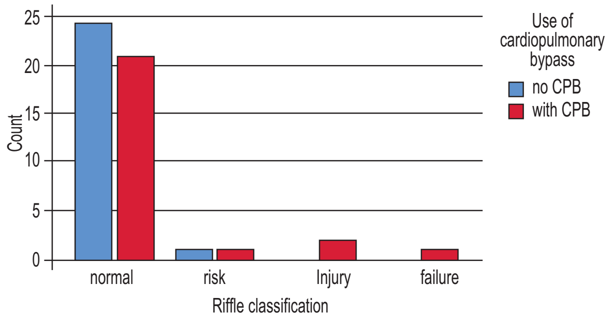

Fig.-1: *Comparison of Rifle classification according to use of cardiopulmonary bypass*

or without use of CPB. However, incidence of RIFLE- injury and failure is higher in CPB group than no CPB group.

ARF occurred in 10 % of patients undergoing CABG irrespective of use of CPB. 2% of patients developed ARF-D. All the patients died, who required RRT. Changes of creatinine was statistically significant in RIFLE-failure ($p<0.05$) compared to normal renal function. Similarly, changes of eGFR are higher in postoperative CABG patients with the in RIFLE- risk, injury & failure. The median preoperative and postoperative estimated GFR were 81.35 mL/min/1.73 m^2 (65.37 to 97.77 mL/min/1.73 m^2), and 60.51 mL/min/1.73 m^2 (39.78 to 81.24 mL/min/1.73 m^2) respectively, the lowest being 10.62 mL/min/1.73 m^2. The median preoperative and postoperative plasma creatinine level were 0.94 mg/dl (0.70 to 1.05 mg/dl), and 1.44 mg/dl (0.4 to 2.4 mg/dl) respectively, the highest being 5.8 mg/dl. Regarding urine output per hour, <0.5 ml/kg/6 hrs. and <0.5 ml/kg/12 hrs. is found in RIFLE-risk and injury patients respectively. Anuria is observed in a patient with RIFLE-failure.

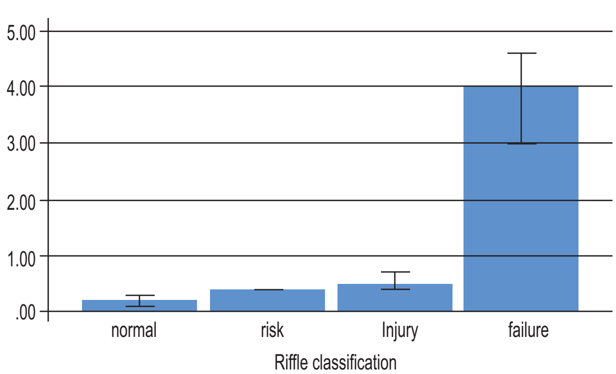

Fig.-2: *Changes of serum creatinine according to RIFLE classififcation*

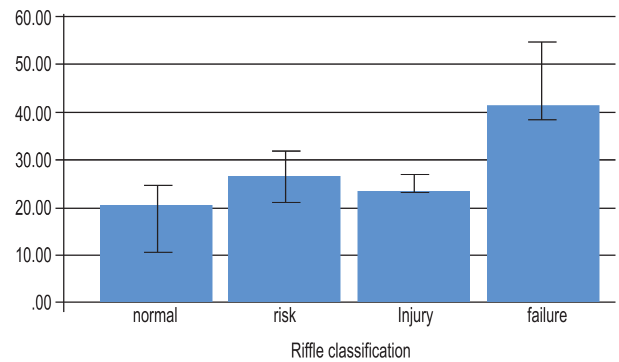

Fig.-3: *Changes of eGFR according to RIFLE classififcation*

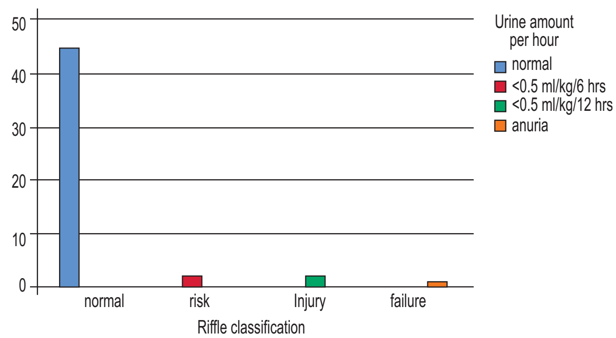

Fig.-4: *Change of urine output according to RIFLE classififcation*

Table III. Shows distribution of patients according to the RIFLE classification. Table III also shows the proportions of RRT, death, and prolonged length of ICU stay (5 days or more) in each RIFLE groups. Using the *Fisher's exact* test, the *p* values are compared to RIFLE-normal.

The postoperative proportions of mortality and RRT for renal failure were 2% (number of patients, 1 of 50) and 2% (1 of 50), respectively. For the whole study cohort, the median postoperative duration of stay in the ICU was 4.0 days, with interquartile ranges of 3.0 to 7.0 days. Patients of ARF especially Rifle classification-injury and failure had higher prolonged length of ICU stay (5 or more days) than RIFLE-normal and Risk.

Table IV: Changes in plasma creatinine, estimated GFR, and urine volume per hour are compared, which are significantly different ($p<0.001$) between dead patients and survivors. The number of patients and their percentages, as well as medians with interquartile ranges, are shown. The Mann-Whitney test/ *Fisher's exact test* yielded the *p* values.

Table-III

Comparison of postoperative variables according to the RIFLE classification

RIFLE level	No (%)	Renal replacement therapy	Mortality	ICU stay (More than 5 days)
Normal	45(90%)	0 (0%)	0 (0%)	0 (0%)
Risk	2 (4%)	0 (0%)	0 (0%)	1 (25%)
Injury	2 (4%)	0 (0%)	0 (0%)	2 (50%)
Failure	1 (2%)	1 (100%)	1 (100%)	1 (25%)
		p<0.001	p<0.001	p<0.05

Table-IV

Comparison of changes in plasma creatinine, estimated GFR, and urine volume per hour between dead patients and survivors

	Alive	Dead	Significance of difference
Change of serum creatinine (mg/dl)	0.2 (0.2-0.4)	3.0 (0.7-4.3)	p<0.001
Change of eGFR (mL · min^{-1} · 1.73 m^{-2})	21 (8-29)	41.25 (30.44-52.54)	p<0.001
Urine amount per hour			
Normal	45 (91.8%)	0 (0.0%)	p<0.001
<0.5 ml/kg/6 hrs.	2 (4.1%)	0 (0.0%)	
<0.5 ml/kg/12 hrs.	2 (4.1%)	0 (0.0%)	
Anuria	0 (0.0%)	1 (100%)	

Discussion:

We observed that ARF following CABG may be categorized using the new consensus criteria in this observational analysis. During ICU stay following CABG, 90% of patients exhibited normal renal function, whereas 10% had renal impairment, according to this definition. Postoperative renal damage has been verified as one of the most dreadful consequences following cardiac surgery. Furthermore, RRT has been linked to a significant rise in mortality. The incidence of ARF after cardiac surgery has varied from 5% to 30%, based on the definition used to delineate the complication, whereas RRT was indicated in 1% to 5% of patients with severe illness. In present study, 2% of patients of ARF required RRT. The results are very identical to earlier studies analyzing consensus criteria for ARF definition in cardiac surgery patients.

Patients in this analysis had 6% in-hospital death rate in the most severe category of ARF, as determined by RIFLE consensus criteria. Death rate related with the postoperative ARF is as much as 60% in certain researches but likely varies from 15 to 30%, based on the criteria of ARF and the time following surgery analyzed (hospital discharge or 30-day mortality).[9] Despite advancements in postoperative critical care and RRT technology, the death rate in patients requiring dialysis is quite significant in all reported investigations, averaging 60 to 70%.[10] In this study, there was no mortality without ARF, however all of the patients with ARF categorized as RIFLE class Failure died in the postoperative period. Chertow et al. in a multivariate analysis observed ARF-D to be potential risk of death rate with an odds ratio of 7.9.[11] The causes of the excess mortality are likely due to pathophysiologic changes-owing to renal impairment and unfavorable consequences of RRT. Volume overload due to salt and water retention, hyperkalemia and acid-base imbalances, hemodynamic instability, visceral ischemia, insulin resistance and excessive protein breakdown, immune dysregulation linked to ARF, platelet dysfunction and high incidence of infections,[1] all these may cause increased death in this group of individuals.

Both the variation in plasma creatinine concentration [3.0 (0.7-4.3)] mg/dl ($p<0.001$) and the change in GFR [41.25 (30.44-52.54)] mL/min/1.73 m^2 ($p<0.001$) have been identified with increased mortality in our study, which are included in the RIFLE criteria. According to Lassnigg et al., patients with a 0 to 0.5-mg/dl and >0.5-mg/dl increase in serum creatinine had 2.77 and 18.64-fold higher 30-day mortality, respectively than individuals whose serum creatinine level has not increased.[12] Thakar et al. also showed similar results in a study, in which death rate reached 5.9% ($P<0.001$) when GFR deteriorated ≥30% but did not necessitate RRT and 0.4% ($p<0.001$) when GFR decreased <30%.[13]

In this study, there is no significant difference in ARF (RIFLE classification-normal and risk) with or without use of CPB. However, occurrence of RIFLE- injury and failure is higher in CPB group than no CPB group. Low flow, low perfusion pressure, hemodilution, variations in body temperature, lack of pulsatile flow. hemolysis (may be due to cardiotomy suction, prolong CPB time, occlusive roller pumps, turbulent flow in the oxygenator, and blood circulation through cell savers), systemic inflammatory response syndrome (may be due to ischemia-reperfusion injury, contact of blood products with extracorporeal bypass circuit, endotoxemia and surgical trauma) are CPB related factors, those may cause postoperative renal impairment.[14] According to Lok et al., individuals who had ARF after CPB had a relative risk of death of 4.6 after one year when compared to those who did not have renal impairment. Patients with ARF-D are often dialysis dependent[1]. In a retrospective study, Leacche et al. observed that 64 percent of ARF-D patients undergoing cardiac surgery with CPB required permanent dialysis, with only 10% surviving 12 months.[1]

The choice of definition for ARF requires further appraisal, as there has been nonexistence of standard criteria to explain ARF. Various indicators of renal tubular injury (α1 microglobulin, glutathione transferase- α, glutathione transferase-pi, N-acetyl-β-D-glucosaminidase), has been illustrated, to recognize subclinical renal dysfunction following cardiac surgery. However, there is no proof that upturn of these indicators is linked to postoperative morbidity or death.[15]

Generally, serum creatinine concentration has been used to define ARF criteria as well as to predict morbidity and death following cardiac surgery.[9] Different studies have used different degrees of aberration in plasma creatinine levels as cutoffs for establishing ARF. Nonetheless, in the non-steady state of ARF, plasma creatinine will not be an accurate representation of GFR since it is affected not only by glomerular function, but also by the function of renal tubules and production of creatinine. As a result, the severity of renal failure may be misinterpreted, as GFR declines and creatinine secretion rises, ultimately reducing the rise in serum creatinine.[16] Because it takes time for creatinine to increase in the circulation, it may rise slowly after bypass because of hemodilution, despite a considerable reduction in GFR. Despite delayed rise, changes in serum creatinine do indicate changes in GFR and they are therefore important to diagnosis ARF. Moreover, a fall in serum creatinine correlates to renal recovery from ARF.[16]

Acute kidney failure is characterized by a steady decline in GFR and/or a temporary and gradual decrease in urine output, which is subsequently exhibited by an elevation of serum creatinine. Although urine output reflects delicate changes in renal function than biochemical indicators, it is seldom reported variable impacting ARF following cardiac surgery.[4] It's worth noting that the difference between the GFR and the rate of tubular reabsorption determines urine output. As a result, if the GFR is low due to chronic renal disease and poor tubular absorption, the patient may initially have adequate urine production. Tubular absorption is adequate at first with a low GFR and then gradually decreases with AKI.[16]

The occurrence of postoperative renal impairment is determined on how it is defined. As a result, a classification system (RIFLE) has been designed to detect the severity of renal failure. Because the kidneys' function includes both the elimination of nitrogenous waste products and the generation of urine, postoperative ARF can be defined using either the creatinine level/GFR or the urine output parameters. These new ARF suggestions have yet to be widely evaluated. Hence, we studied the validity of this new consensus criteria after CABG.

Conclusion:

The renal impairment is there still one of the most serious complications and may be used to determine severity of disease. Despite all attempts, clinical outcomes are dismal, as evidenced by the current study, which identified that ARF was directly linked to mortality and longer ICU stays. The RIFLE classification furnishes reasonably accurate definition of postoperative acute kidney failure. RIFLE class injury and failure are independently linked to prolonged length of ICU stay and in-hospital mortality. The current study' s findings indicated that there is a substantial link between postoperative ARF as defined by new consensus criteria and mortality. Thus, surgeons can diagnose and classify patients with an elevated risk of mortality owing to renal impairment following CABG by establishing the RIFLE level.

Conflict of Interest - None.

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