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Acute Kidney Injury in the Intensive Care Unit According to the RIFLE

Yoğun Bakımda Akut Böbrek Hasarının RIFLE Sınıflaması ile Değerlendirilmesi

Azime BULUT[1], Oktay DEMİRKIRAN[2]

[1]Giresun University Faculty of Medicine, Department of Anesthesiology and Reanimation, Giresun, Türkiye
[2]İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, Department of Anesthesiology and Reanimation, İstanbul, Türkiye

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ABSTRACT

Objective: The RIFLE classification is widely used to decide when to start renal replacement therapy (RRT) in patients with acute kidney injury (AKI). In this study, we aimed to examine the frequency, etiology, and effects of mortality and morbidity of AKI in intensive care unit (ICU), and whether the timing of continuous RRT is associated with survival using the RIFLE classification.

Methods: Two hundred-ninety one patients hospitalized in the ICU between 2012 and 2013 were retrospectively analyzed after the approval of the ethics committee. Patients with previous kidney failure or kidney transplantation, those under the age of 18, and those who were hospitalized in the ICU for 24 h were excluded from the study. The clinical, laboratory, and demographic data of the patients and their survival were evaluated.

Results: AKI was detected in 27% (n=67) of 244 patients, according to the RIFLE classification, within the first 24 h of admission to the ICU. While 47.7% (n=32) of 67 patients were followed up with sepsis and 52.2% (n=35) had non-sepsis causes. While patients with AKI had 64.1% mortality, the mortality of patients without AKI was 25.9%. There was also a significant difference in mortality between the RIFLE stages. It was correlated with the Acute Physiological and Chronic Health Evaluation-II score.

Conclusion: RIFLE classification can predict hospital mortality and short-term prognosis in patients with sepsis in the ICU.

Keywords: RIFLE, acute kidney damage, renal replacement therapy

ÖZ

Amaç: RIFLE sınıflaması, akut böbrek hasarı (ABH) olan hastalarda renal replasman tedavisine (RRT) ne zaman başlanacağına karar vermede yaygın olarak kullanılmaktadır. Bu çalışmada, yoğun bakım ünitesi (YBÜ) ABH'nin sıklığını, etiyolojisini, mortalite ve morbiditeye etkilerini ve sürekli RRT zamanlamasının sağkalım ile ilişkisini RIFLE sınıflamasını kullanarak incelemeyi amaçladık.

Yöntem: 2012-2013 yılları arasında YBÜ'de yatan 291 hasta etik kurul onayı alındıktan sonra retrospektif olarak incelendi. Daha önce böbrek yetmezliği veya böbrek nakli olan hastalar ile 18 yaş altı ve YBÜ'de 24 saatten daha az yatan hastalar çalışma dışı bırakıldı. Hastaların klinik, laboratuvar ve demografik verileri ve sağkalımları değerlendirildi.

Bulgular: RIFLE sınıflamasına göre 244 hastanın %27'sinde (n=67) YBÜ'ye yatıştan sonraki ilk 24 saat içinde ABH saptandı. Altmış yedi hastanın %47,7'si (n=32) sepsis ile izlenirken, %52,2'si (n=35) sepsis dışı nedenlerle yatırılmıştı. ABH olan hastalarda mortalite %64,1 iken, ABH olmayan hastalarda mortalite %25,9 idi. RIFLE evreleri arasında mortalite açısından anlamlı fark vardı. Akut Fizyolojik ve Kronik Sağlık Değerlendirmesi-II skoru ile korele idi.

Sonuç: RIFLE sınıflaması, YBÜ hastalarında hastane mortalitesi ve kısa dönem prognoz için tahmin sağlayabilir. Ayrıca RRT'de zamanlama kararı için yol gösterici olabilir.

Anahtar Kelimeler: RIFLE, akut böbrek hasarı, renal replasman tedavisi

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Corresponding Author/ Sorumlu Yazar:

Azime BULUT MD

Giresun University Faculty of Medicine, Department of Anesthesiology and Reanimation, Giresun, Türkiye

Phone: +90 533 545 13 24

cimemazime@yahoo.com.tr

ORCID: 0000-0001-8164-5617

INTRODUCTION

Acute kidney injury (AKI) is a syndrome that occurs because of sudden deterioration in kidney function and has a prevalence exceeding 50% in intensive care units (ICU).[1] Risk, Injury, Failure, Loss, and End-stage renal failure (RIFLE) and AKI network classifications have been developed for the diagnosis of AKI. Both are associated with an increase in serum creatinine levels and a decrease in glomerular filtration rate and urinary output.

It has been suggested that the RIFLE classification has a high predictive quality of survival and is a guide for determining the improvement of renal function, the need for continuous renal replacement therapy (RRT), length of hospital stay, mortality, and morbidity.[2]

To be able to stage according to the RIFLE classification and follow the degree of damage, it is necessary to insert a urinary catheter or to know the basal creatinine value and measure it regularly. While making the RIFLE classification on the basis of urine output, errors and limitations are created in the evaluation of the patients' fluid balance, whether diuretics are used or not. If the basal creatinine value is taken as a basis and if the basal creatinine value is not known, it creates a problem. These are disadvantageous situations for RIFLE classification.

In this study, we aimed to evaluate the association between RIFLE score on the first day of admission and sepsis, mechanical ventilation requirement, transfusion requirement, vasoactive support, mortality, and morbidity in patients hospitalized in the emergency ICU. In addition, we analyzed the relationship between the time of initiation of continuous RRT and survival using the RIFLE classification.

METHODS

Our study was conducted in the Emergency Intensive Care Unit of Cerrahpaşa Faculty of Medicine Hospital, Department of Anesthesiology and Reanimation, in accordance with the Declaration of Helsinki, with the approval of the İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine Ethics Committee (document number: 604/02-6280, date: 11 March 2014). The study was planned as a retrospective, observational study. We examined the medical records of 291 patients admitted to the ICU from January 2012 to December 2013.

Patients

The reason for admission to the ICU, gender, age, body weight, co-morbidities, Acute Physiological and Chronic Health Evaluation-II (APACHE-II) scores, RIFLE stage on the first day of hospitalization, length of stay, and mortality of the patients were recorded. We evaluated the stage at which RRT was initiated during the ICU stay. The mortality of these patients according to their stage was recorded. Patients under the age of 18 years who were hospitalized in the ICU for less than 24 h and those with a previous history of chronic kidney failure were excluded.

When calculating the RIFLE stage of the patients, the worse stage was accepted according to creatinine or urine output. The creatinine value estimated using the Modification of Diet in Renal Disease equation was accepted as baseline creatinine for patients whose baseline creatinine value was unknown and had no history of renal disease.

When examining the relationship between the initiation stage of RRT and mortality, we excluded patients who received RRT for reasons other than AKI.

Statistical Analysis

Number Cruncher Statistical System 2007 and Power Analysis and Sample Size 2008 statistical software was used for statistical analysis. Student's t-test, Mann-Whitney U test, and Kruskal-Wallis test were used. Significance was evaluated at $p<0.01$ and $p<0.05$ levels.

RESULTS

Two hundred-forty four adult patients were included in the study. According to the RIFLE classification, the AKI and non-AKI groups consisted of 67 (27%) and 177 (73%), respectively. The mean age of patients with AKI was 66.8 years, which was significantly higher than that of patients without AKI (60.7 years, $p<0.05$). Of the patients who developed AKI, 28 (45%) were female and 39 (55%) were male. There was no statistically significant difference between genders in terms of AKI ($p>0.01$). The AKI group was also classified according to RIFLE as follows: risk (n=10, 4.1%) injury (n=20, 8.2%) and failure (n=35, 14.3%) and reminders were in loss (n=2, 0.8%) and end-stage renal disease (n=0) (Table 1).

The length of ICU stay of patients with AKI was found to be statistically significantly different when compared with that of patients without AKI ($p<0.01$). AKI significantly increases the length of stay in the ICU.

The patients were evaluated in terms of hypertension, diabetes, and malignancy history, which are thought to affect the development of AKI. The rates of diabetes or hypertension did not show a statistically significant difference according to the incidence of AKI ($p>0.05$). While no statistically significant difference was found between the history of malignancy and the development of AKI ($p>0.05$), the rate of the presence of malignancy in patients with AKI was higher than that in patients without AKI.

When the incidence of sepsis in patients with AKI was examined, a statistically significant difference was found

compared with that in patients without AKI (p<0.05). The incidence of sepsis is 4.46 times higher in patients with AKI.

The duration of stay on mechanical ventilation of patients with AKI was compared with those without AKI, and no statistically significant difference was found (p>0.05). Mechanical ventilation times of patients with and without AKI were found to be similar.

The need for vasoactives and blood transfusion was found to be associated with the presence of kidney damage (p<0.01). The length of stay of the patients was examined, and it was observed that patients with AKI spent longer time in the ICU compared with those without AKI (p<0.01).

RIFLE and Mortality

Of all 244 patients, 155 (63.5%) were discharged from the service, and 89 (36.5%) died in the ICU. According to the RIFLE stage on the first day of hospitalization, 43 (64.1%) patients with AKI and 46 (25.9%) patients without AKI were found to be dead. The rate of death in cases with AKI is 6.69 times higher than that in patients who had no AKI on the first day. When we examined cases with AKI in terms of mortality, we found that the mortality rate was higher in the injury and failure stages than in the other stages (Table 2).

It was observed that APACHE-II scores on the day of hospitalization, which are valuable in the estimation of

Table 1. Characteristics of the patients

Characteristics	Without AKI (n=177)	With AKI (n=67)	p value
Age (years)	60.72±18.83	66.84±15.6	0.01[a]
Gender (male)	98 (55.4)	39 (58.3)	0.49[b]
Length of stay (days)	8.61±12.95	12.09±13.33	0.002[c]
Preexisting conditions yes/(%) Hypertension Diabetes mellitus Malignancy	 74 (41.9) 42 (23.8) 53 (30)	 29 (43.3) 22 (32.9) 27 (40.3)	 0.83[b] 0.14[b] 0.12[b]
Clinical condition at follow-up Sepsis Blood transfusion Vasoactive support Mechanical ventilation (days)	 39 (22.1) 96 (54.3) 45 (25.5) 7.93±9.76	 32 (47.7) 58 (86.5) 46 (68.7) 7.98±7.08	 0.01[b] 0,001[b] 0.001[b] 0.23[c]
Mortality (non-survivors)	46 (25.9%)	43 (64.2%)	0.001[b]
The admission category Acute respiratory failure Sepsis Postoperative care Neurological causes Hemorrhagic shock Post-CPR Multitrauma Others	All patients (n=244) 75 (30.7%) 74 (30.3%) 37 (15.1%) 13 (5.3%) 12 (4.9%) 10 (4.1%) 7 (2.9%) 16 (6.7%)		

[a]Student's t-test, [b]chi-squared test, [c]Mann-Whitney U test.
AKI: Acute kidney injury

Table 2. Evaluation of mortality by RIFLE stage on the first day of admission

	Survivors		Non-survivors		p[a] value
	n	%	n	%	
AKI (-)	131	74	46	26	0.001
Risk	5	50	5	50	
Injury	6	30	14	70	
Failure	12	34.3	23	65.7	
Loss	1	50	1	50	
End stage	0		0		

[a]Fisher-Freeman-Halton test.
AKI: Acute kidney injury

mortality and morbidity, have a significant relationship with kidney damage (p<0.05). The APACHE-II scores of patients who died were significantly higher than those who were discharged (p<0.01). When the worst RIFLE stages of the patients in the first 24 h were examined, a statistically significant difference was found between the stages in terms of mortality (p<0.01). As the RIFLE stage progresses, the rate of death increases. We performed pairwise comparisons to determine the stage that creates the difference. We found that the APACHE-II scores of cases without AKI were significantly lower than those with stages R, I, and F. No statistically significant difference was found between the other stages in terms of APACHE-II scores (Table 3).

Renal Replacement Therapy

We have an algorithm that we use before the initiation of RRT in our ICU (Figure 1). After evaluating the clinical situation and RIFLE score together, we decided whether to initiate RRT or not. Thirty-one of 67 patients who had AKI according to RIFLE stage on the first day of hospitalization were not treated with RRT. Because their life expectancy was very low or a rapid improvement in acute kidney damage was foreseen. As a result, in addition to the other 36 patients with AKI, 6 patients without AKI on the first day received RRT because of the development of AKI during their ICU stay.

Sub-group Analysis

We evaluated the records of all 42 patients who received RRT during their ICU stay. We examined the RIFLE stages of these patients at the initiation of RRT. Six patients were at the injury stage, 34 patients were at the failure stage, and 2 patients were at the loss stage. We analyzed these patients to determine the relationship between RIFLE stages at the time of RRT initiation and survival. However, it could not be statistically evaluated whether early initiation had a positive effect on mortality or not due to the insufficient number of patients.

DISCUSSION

AKI is an important condition that worsens the prognosis of patients in the ICU. It is directly related to mortality. The importance of early detection of AKI and applying treatments with appropriate measures has led to the development of many scoring systems. We evaluated the association between AKI and mortality, RRT need, and timing of RRT in this study. We found that mortality was higher in patients who had AKI according to the RIFLE on the first day of admission. In addition, we determined if there was a relationship between mortality and the timing of RRT. However, we could not examine this because of the insufficient number of patients.

Because AKI often occurs secondary to conditions such as sepsis and trauma in patients hospitalized in the ICU, it was thought that mortality was not due to AKI but to the underlying disease.[3] However, it has long been accepted that AKI is an independent risk factor for mortality and a complication of critical illness.[4]

The most common causes of AKI in the ICU are sepsis and septic shock. While the frequency rates vary between 1-31%, the mortality rates are observed to be between 28-82%.[5,6] The reason for this wide distribution is due to the differences in criteria for diagnosing AKI. With the need arising from this confusion, the RIFLE classification was created in 2004.[7] Although the dynamic efficiency of the RIFLE staging system is based on the patient's highest value regardless of time, it is a very sensitive classification in the recognition of AKI. With this classification, awareness of possible AKI could be increased, early diagnosis could be ensured, and the possibility of using a common language in international studies for AKI was created. Although the RIFLE classification was created primarily to standardize the definition and staging of AKI rather than to predict mortality, many studies have shown that mortality increases significantly when there is an increase from Risk to Injury according to RIFLE.[8-10] In our study, the ICU mortality in patients with AKI according to RIFLE classification was

Table 3. Evaluation of APACHE-II scores according to the RIFLE stages on the first day of admission

		APACHE-II scores		p[a] value
	Number of patients	Mean±SD	Median	
AKI (-)	177	16.95±6.20	16.0	**0.001**** **Post-hocs:** **1 <2, 3, 4**
Risk	10	24.00±8.25	22.0	
Injury	20	24.15±8.16	24.5	
Failure	35	24.74±7.92	23.0	
Loss	2	22.50±0.71	22.5	
End stage	0	0	0	

[a]Kruskal-Wallis test, [b]Mann-Whitney U test, **p<0.01.
AKI: Acute kidney injury, APACHE-II: Acute Physiological and Chronic Health Evaluation-II, SD: Standard deviation

64.2% (43/67), which was statistically significantly higher than that in patients without AKI.

Although there are studies on whether AKI is affected by gender difference and showing that female gender is protective for renal ischemia, many studies have also reported that there is no difference.[11,12] In our study, no significant relationship was found between gender and the frequency of AKI (p=0.49, p>0.01). It has been reported in many publications that the frequency of AKI increases with age.[7-12] In our study, in the comparison between age and RIFLE classification, it was determined that the increase in age significantly (p<0.05) increased the rate of damage and failure.

The effectiveness of diabetes and hypertension on the development of AKI has been examined in many studies, and a significant relationship has been found between them.[13] In our study, no significant relationship was found between diabetes or hypertension and the frequency of AKI. It was thought that this result, which was incompatible with the literature data, might be due to the lack of patient records.

Prolongation of the length of stay in the ICU is closely related to advanced organ damage. In the study by Chertow et al.[14], published in 2005, the effects of AKI on hospitalization, mortality, and cost were investigated. In this study, it was shown that each 0.5 mg/dL increase in creatinine level increases the length of stay by approximately 3.5 days. In our study, as the incidence of AKI increased, the length of stay also increased.

In our study, the APACHE-II score, which is known to be correlated with mortality, was calculated in all patients. A highly significant difference was found between mortality and APACHE-II (p=0.001; p<0.01). When its relationship with AKI was examined, it was shown that an increase in the APACHE-II score was associated with an increase in the RIFLE stage. Similarly, in a multicenter study in which 8,639 patients were included and the incidence of AKI was found to be 32.9%, there was a statistically significant relationship between AKI and APACHE-II scores.[15]

Although there are studies showing that early initiation of RRT decreases mortality, there are also publications showing that late initiation of RRT does not have a negative

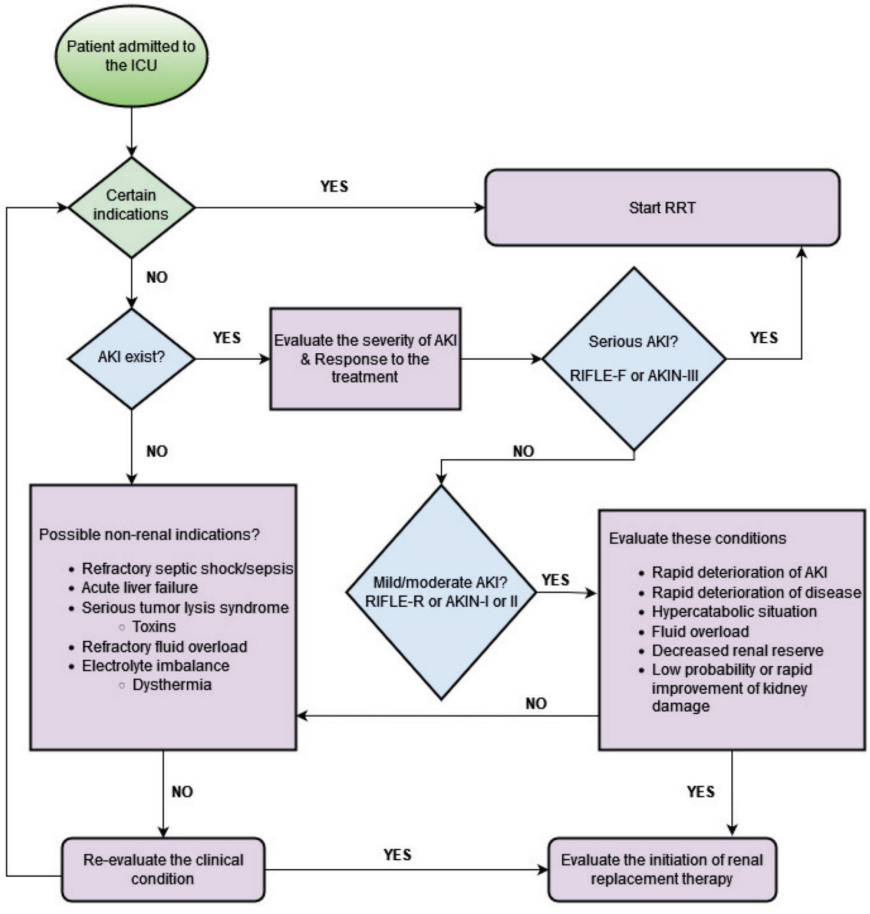

Figure 1. Algorithm for initiating renal replacement therapy

ICU: Intensive care unit, RRT: Renal replacement therapy, AKI: Acute kidney injury, AKIN: AKI network

effect on mortality.[16,17] According to the BEST Kidney Study, the most common indications for RRT were oliguria or anuria (70.2%), high urea/creatinine levels (53%), metabolic acidosis (43.6%), and fluid overload (36.7%).[18] According to the same study, the criteria for initiating RRT vary according to region and country. While it started early in Australia and European countries, this period was later in North and South America.

In our ICU, we use an algorithm to decide the initiation of RRT (Figure 1). Accordingly, RRT is started immediately in our patients with RIFLE stage F and in patients with RIFLE stage R or I when there are additional conditions that worsen the condition. Accordingly, RRT was not applied to 31 of 67 patients with AKI according to the RIFLE stage on the first day. In other words, RRT was applied to the remaining 36 patients either immediately during their admission to the ICU or because of the worsening stage in their follow-up. In addition, 6 patients were taken to RRT because there was no AKI on the first day, but there was AKI in their follow-up. Therefore, RRT was applied to 42 patients. We evaluated these patients to determine whether there was a significant difference between the RIFLE stages at the time of initiation of continuous RRT and survival. However, we could not conclude due to the insufficient number of patients.

Study Limitations

The study had several limitations. First, because the study was designed retrospectively, precise accurate information about the history of the patients may not be obtained. Second, the fact that the patients are not homogeneous makes it difficult to determine the effect of AKI on mortality alone. Larger groups of patients are needed to examine the effect of RRT on mortality to the RIFLE stage.

CONCLUSION

AKI is an important cause of mortality and morbidity in critically ill patients. The RIFLE classification provides valuable information regarding kidney function, and we believe that the RIFLE staging system is a practical scoring system. We believe that the use of RIFLE classification in the ICU will increase awareness of AKI and therefore decrease mortality.

Ethics

Ethics Committee Approval: The study was approved by the İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine Ethics Committee (document number: 604/02-6280, date: 11 March 2014).

Informed Consent: Retrospective study.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: O.D., Concept: O.D., Design: A.B., Data Collection or Processing: A.B., O.D., Analysis or Interpretation: A.B., Literature Search: A.B., Writing: A.B.

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