Factors Affecting Acute Renal Failure in Intensive Care Unit and Effect of These Factors on Mortality

Yoğun Bakım Ünitesine Yatan Hastalarda Akut Böbrek Yetmezliği Gelişimi Üzerine Etkili Faktörler ve Bu Faktörlerin Mortalite Üzerine Etkileri

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ABSTRACT Objective: Early detecting acute renal failure is important by the aspect of determination of the disease's severity and grade of the organ dysfunction. The Acute Dialysis Quality Initiative workgroup designed a classification system for acute kidney injury (AKI) named as the RIFLE (Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease). The aim of our study is to assess acute renal failure development in intensive care units patients, factors affecting it and the effect of the factors over mortality via using RIFLE score. **Material and Methods:** The age, height, weight, gender, diagnosis, comorbid diseases, admission reason to the intensive care, intensive care stay, the APACHE II score, SOFA score, RIFLE score, biochemical parameters (albumin, prealbumin, urea, creatinine, cholesterol, HCO3 level), triceps thickness and waist circumference measurement were all recorded. Patients were grouped into AKI and non-AKI. The AKI group was assessed by RIFLE score due to hourly urine output and creatinine rise separated into three groups as R=Risk, I=Injury, F=Failure. **Results:** 502 patients were enrolled to the study. 39,2% of the patients was in the acute kidney injury group while 60.8% was in non- acute kidney injury group. The renal failure development is related with high age, short body height, excessive weight, existence of chronic disease and long intensive care units hospitalization period. **Conclusion:** In conclusion, patients with high age, excessive weight, chronic diseases, high urea, creatinine, HCO3- levels, low cholesterol, albumine and prealbumine levels are prone to renal failure.

Key Words: Acute kidney injury; RIFLE protein, rat; waist circumference

ÖZET Amaç: Akut böbrek yetmezliğinin erken dönemde tespiti hastalığın şiddetinin belirlenmesi ve organ yetmezliğinin sınıflandırılması açısından önemlidir. Akut Diyaliz Kalite Çalışma Grubu akut böbrek hasarı (AKI) sınıflandırılması için RIFLE (risk, hasar, yetmezlik, kayıp, son dönem böbrek yetmezliği) adı verilen bir klasifikasyon sistemi geliştirmiştir. Bu çalışmada amaç yoğun bakım hastalarında RIFLE skoru kullanılarak akut böbrek yetmezliği gelişimini incelemek ve gelişiminde etkili olan faktörleri araştırmaktır. **Gereç ve Yöntemler:** Yaş, boy, vücut ağırlığı, cinsiyet, tanı, ek hastalıklar, yoğun bakıma yatış nedeni, yoğun bakım kalış süresi, APACHE II skoru, SOFA skoru, RIFLE skoru, biyokimyasal parametreler (albumin, prealbumin, üre, kreatinin, kolesterol, HCO3 değerleri), triseps kalınlığı ve bel kalınlığı kayıt edildi. Hastalar AKI ve AKI gelişmeyen şeklinde sınıflandırıldı. AKI grubu RIFLE sınıflaması kullanılarak ve saatlik idrar çıkışı takip edilerek R: risk, I: Hasar ve F: Yetmezlik şeklinde ayrıldı. **Bulgular:** Çalışmaya 502 hasta dahil edildi. Hastaların %39,2'si AKI grubunda iken, %60,8'i AKI gelişmeyen grupta idi. Akut böbrek yetmezliği gelişmesi ileri yaş, kısa boy, kilo fazlalığı, kronik hastalık varlığı ve uzun yoğun bakım yatış süresi ile ilişkili bulundu. **Sonuç:** Sonuç olarak, ileri yaşı olan, fazla kilolu, kronik hastalığı olan, yüksek üre, yüksek kreatinin, yüksek HCO3- değerleri olan, düşük kolesterol, düşük albumin ve düşük prealbumin değerleri olan hastalarda böbrek yetmezliğinini daha sıklıkla olabileceğini düşünmekteyiz.

Anahtar Kelimeler: Akut böbrek hasarı; RIFLE protein, rat; bel çevresi

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Acute renal failure (ARF) is decreased glomerular filtration rate (GFR) which is a situation that accumulation of the blood urea nitrogen, creatinine and other uremic toxins in the body.[1] Loss of renal function is accompanies metabolic acidosis, fluid and electrolyte disorders, and thus affect many organ systems.[2,3] Mortality of patients with acute renal failure were significantly higher than without renal failure, and varies between 35-75%.[3-5]

Acute Dialysis Quality Initiative (ADQI) work group, designed a classification system for acute kidney injury (AKI) in 2004 as named as the "RIFLE" classification. This classification system depends on the severity of illness and divided to Risk (class R), Injury (class I), Failure (class F), Loss (class F) and End-stage kidney disease (class E).[6-8] RIFLE system classificate the severity of AKI focused on changes of serum creatinine or urine output from the baseline condition.[6] RIFLE criteria is a simple and convenient classification for categorizing ARF and predict the likelihood of developing ARF.[9-12]

RIFLE classification, several instruments to evaluate renal dysfunction and mortality, such as the Sequential Organ Failure Assessment (SOFA) and Acute Physiology and Chronic Health Evaluation (APACHE) II are used in intensive care unit patients.[13-15]

Other than scoring systems, the anthropometric measurements and biochemical parameters that affect the development of ARF are also available. In studies in which patients with renal failure are included, parameters such as body mass index, abdominal circumference, skin fold thickness may predict the development of renal failure.[16-19]

Among the biochemical tests, urea and creatinine are the primary laboratory tests in patients at risk of developing acute renal failure. Outside of these tests, publications in the literature are shown to be a relationship between the development of renal failure and albumin, prealbumin, HCO_3 and total cholesterol levels.[20-23]

In our study, we aimed to determine the incidence of ARF according to RIFLE classification on the patients in intensive care units followed with different diagnoses, and to compare the effect of intensive care unit scoring systems (SOFA and APACHE II), anthropometric measurements (height, weight, waist circumference, triceps thickness) and biochemical parameters (blood urea nitrogen, creatinine, albumin, prealbumin, HCO_3 and total cholesterol) with the development of ARF and mortality.

MATERIAL AND METHODS

Following the Faculty Ethics Committee's approval, the study took place in Surgical Intensive Care (12 bedspace) and Reanimation Intensive Care (7 bedspace). After the signed approval of all the participants or their legal representatives between March 26, 2012 and March 26, 2013, this study began with 502 patients staying in the intensive care unit for more than 24 hours out of 1059 patients over 18 who were admitted there.

The exclusion criteria as were follows: patients under 18 years old, patients who refused to take part in the study, the pregnant patients, patients with brain death, patients stayed less than 24 hours in the intensive care and patients with diagnosed chronic renal diseases.

The age, height, weight, gender, diagnosis, comorbid diseases, admission reason to the intensive care and intensive care stay were recorded. Also in the first day, in the seventh day and in the 14.day after admission to the intensive care, the APACHE II score, SOFA score, RIFLE score, biochemical parameters (albumin, prealbumin, urea, creatinin, cholesterol, HCO_3^- level), triceps thickness and waist circumference measurement were all recorded. The triceps thickness was measured by using Economy Plastic Skinfold Caliper.

Patients were classified into acute kidney ınjury (AKI) and non-acute kidney ınjury (non-AKI). Patients in non-AKI group had no oliguria and obvious creatinine rise, while patients in AKI group had oliguria and obvious creatinine rise. The AKI group was assessed by RIFLE score due to hourly urine output, creatinine rise and separated into three groups as R=Risk, I=Injury, F=Failure. The RIFLE system was focused on the worst values of

either glomerular filtration rate or urine output. In our study, changes in serum creatinine level and urine output were used to classify patients using the RIFLE criteria.[6] All the patients was classified by the highest RIFLE score during two weeks period of intensive care units hospitalization.

The patients were followed up until they were discharged from the intensive care unit or died. The duration of stay in the intensive care and duration of mechanical ventilator were all recorded.

STATISTICAL ANALYSIS

The findings obtained at the end of the study were evaluated in the Biostatistics Department of Trakya University Medical Faculty. The statistical assessment was carried out by using the 10240642 licensed-coded SPSS 20 statistics program. After the convenience of commensurable data to the normal distribution was assessed through single sample Kolmogorov Smirnov test, variance analysis and post-hoc Bonferroni test were carried out in intergroup comparisons for normal distributions, while Kruskal-Wallis variance analysis and Mann Whitney U were conducted in the comparisons for those who didn't show normal distribution. Pearson χ^2 test was preferred for qualitative data. As for the descriptive statistics, Median (Min-Max) values and arithmetic mean±standard deviation were provided. For all the statistics, the significance limit was $p<0.05$, and for Mann Whitney U test results which are used after the Kruskal-Wallis variance analysis, $p<0.017$ was selected by revising with Bonferroni.

RESULTS

60.8% of the patients was in non AKI group while 39.2% was in AKI group. There was statistically difference between non-AKI and AKI groups according to age, height and weight ($p<0.05$) (Table 1).

The diagnosis of the patients according to groups was shown in Table 2. In the non AKI group the most patient diagnosis was malignancies while neurologic diseases in AKI group. Statistically difference was detected between groups on comorbid diseases ($p<0.05$).

The duration of stay was longer in AKI group and statistically difference was detected between groups ($p=0.001$). In the subgroups of AKI, the duration of stay in intensive care was longer in Injury and Failure groups than Risk group ($p<0,05$). There was no statistically difference between Injury and Failure groups ($p>0.05$) (Table 3). In the AKI group the APACHE II score was found as 24.3±9, the SOFA score was found 8,5±4, and in the non-AKI group the APACHE II score was found as 13.6±8.6 and the SOFA score was found as 4.4±3.3 ($p=0.001$) (Table 3).

In the AKI group, the triceps thickness measurement was 14.7±6.8 mm while 13.6±6.3 mm in non-AKI group ($p>0.05$). The waist circumference measurements in AKI group was 97.6±18.7 cm and 92.4±14.0 cm in non-AKI group. The waist circumference measurement is longer in AKI group, and statistically difference was detected ($p=0.0001$) (Table 3).

TABLE 1: Demographic data.

	non-AKI n=305 60.8%	AKI n=197 39.2%	AKI			p
			Risk	Injury	Failure	
Age (year)	57.5±18.5	67.1±15.1	67.1±15.1	70.9±12.8	67.1±14.9	0.000[m]
Gender						
Female	143	96	53	30	13	0.686[x2]
Male	162	101	54	32	15	
Height (kg)	165.3±10.0	163.3±9.8	163.7±10.3	162.8±9.0	162.9±9.8	0.026
Weight (cm)	78.1±7.1	80.0±20.04	79.2±21.3	81.5±20.3	80.0±17.5	0.027[m]

[m]: Mann Whitney U test; [x2]: Chi square test; AKI: Acute kidney injury.

TABLE 2: Diagnosis according to groups (%).

		Non-AKI	AKI			Total AKI	p
			Risk	Injury	Failure		
Diagnosis	Respiratory diseases	6.2	15	16.1	21.4	16.2	
	Gastroenterologic diseases	13.8	19.6	14.5	21.4	18.3	
	Cardiovascular illness	3.9	7.5	12.9	14.3	10.2	
	Malignancy	24.3	15	17.7	14.3	15.7	
	Infection	3.0	4.7	6.5	10.7	6.1	
	Neurologic diseases	15.7	24.3	22.6	10.7	21.8	
	Trauma	18.4	8.4	8.1	3.6	7.6	
	Other	14.8	5.6	1.6	3.6	4.1	
Comorbid diseases	Diabetes Mellitus	2.0	1.9	3.2	3.6	2.5	0.042*
	Hypertension	13.8	9.3	9.7	14.3	10.2	
	Stroke	2.3	5.6	4.8	7.1	5.6	
	Other	7.5	13.1	21.0	14.3	15.7	

* p<0.005.

TABLE 3: Duration of stay, APACHE II, SOFA, triceps thickness and waist circumference measurements.

	Non-AKI (mean±sd)	AKI (mean±sd)	AKI			p
			Risk (mean±sd)	Injury (mean±sd)	Failure (mean±sd)	
Duration of stay (day)	6.2 ± 9.4	14.6±14.6	12.6±14.0	17.0±16.3	16.7±11.7	0.000[m]
APACHE II	13.6±8.6	24.3±9.0	21.0±8.5	27.1±7.9	30.7±7.6	0.000[m]
SOFA	4.4±3.3	8.5±4.0	6.9±3.7	9.5±3.2	12.4±3.2	0.000[m]
Triceps thickness (mm)	13.6±6.3	14.7±6.8	14.7±6.4	15.2±7.0	13.7±7.7	0.057[m]
Waist circumference (cm)	92.4±14.0	97.6±18.7	97.2±18.3	97.6±20.1	99.1±17.3	0.000[l]

[m]: Mann-Whitney U test; [l]: Independent samples t test; APACHE: Acute physiology and chronic health evaluation system; SOFA: Sequental organ failure assessment.

TABLE 4: Biochemical values.

	Non-AKI (mean±sd)	AKI (mean±sd)	AKI			p
			Risk (mean±sd)	Injury (mean±sd)	Failure (mean±sd)	
Urea (mg/dl)	51.8±102.0	98.8±72.0	69.8±49.7	119.3±74.9	164.3±80.8	0.000[m]
Creatinine (mg/dl)	0.8±0.4	1.4±1.0	1.1±0.6	1.7±1.2	2.1±0.9	0.000[m]
Prealbumin (mg/dl)	15.6±6.7	11.6±6.1	12.8±6.6	10.0±4.5	10.2±6.3	0.000[m]
Albumin (mg/dl)	3.1±0.7	2.8±0.7	2.9±0.6	2.7±0.7	2.6±0.6	0.001[l]
HCO_3 (mEq/L)	21.0±4.6	21.9±5.7	22.6±5.3	21.7±6.7	19.8±4.2	0.020[m]
Cholesterol (mg/dl)	129.3±40.1	122.9±39.2	126.6±41.0	120.0±35.6	115.3±39.3	0.064[m]

[m]: Mann-Whitney U test; [l]: Independent samples t test.

The urea (98.8±72.0 mg/dl vs 51.8±102 mg/dl), creatinine (1.4±1.0 mg/dl vs 0.8±0.4 mg/dl), prealbumin (11.6±6.1 mg/dl vs 15.6±6.7 mg/dl), albumin (2.8±0.7 g/dl vs 3.1±0.7 g/dl) and HCO_3^- (21.9±5.7 mEq/L vs 21.0±4.6 mEq/L) measurements were different in each group (p<0.05) (Table 4). The cholesterol values (122.9±39.2 mg/dl vs 129.3±40.1 mg/dl) were similar (p>0.05) (Table 4).

Then the patients were divided into survivors and non-survivors. 65.7% of the patients discharged from the hospital and 34.3% was died. Statistically difference was detected between groups (p=0.0001) (Table 5).

The mean age of the patients in survivors group was 58.5±18.5 years old, while 66.6±15.3 years in non-survivors group (p<0.05). No statistically significant difference detected on gender and height (p>0.05). The weight (76.1±18.5 kg vs 84.2±17.3 kg) and the duration of intensive care stay (6.4±9.1 days vs 15.5±15.3 days) were different (p<0.05) (Table 6).

The comorbidies, urea (52.5±99.2 mg/dl vs 104.5±72.5 mg/dl), creatinine (0.9±0.5 mg/dl vs 1.5±1.0 mg/dl), albumin (3.1±0.7 g/dl vs 2.7±0.7 g/dl), prealbumin (15.8±6.7 mg/dl vs 10.5±5.5 mg/dl) and cholesterol (129.2±38.8 mg/dl vs 122.1±41.4 mg/dl) levels were different between groups (p<0.05) (Table 7). No statistically significant difference was detected between groups on $HC0_3$ levels between groups (p>0.05). Also statistically significant difference was detected between groups on the APACHE, SOFA scores and the waist circumference measurements (p<0.05). There was no statistically significant difference on triceps thickness measurement between groups (p>0.05) (Table 7).

DISCUSSION

In our study, our aim was to determine the incidence of ARF according to RIFLE classification on the patients in intensive care units followed with different diagnoses, and to compare the effects of intensive care unit scoring systems (SOFA and APACHE II), anthropometric measurements (height, weight, waist circumference, triceps thickness) and biochemical parameters (blood urea nitrogen, creatinine, albumin, prealbumin, HCO_3 and total cholesterol) with the development of ARF and mortality.

There are different studies in the literature about the incidence of ARF.[4,5,23-25] Hoste et al. reported 67% for ARF.[6] The authors reported 12% for risk, 27% for injury and 28% for failure. Gomez et al. reported 50% incidence for ARF in trauma patients and 24% for risk, 18% for injury and 37.8% for failure.[7] Park et al. reported the incidence of ARF as 41.3 % on 378 patients.[24] The authors found

TABLE 5: Hospital discharge and mortality of groups.

		Survivors n=330 65,7%		Non-survivors n=172 34,3%		p
		n	%	n	%	
Non-AKI		259	78.5	46	26.7	0.000^{X2}
	Risk	56	17.0	51	29.7	
AKI	Injury	13	3.9	49	28.5	
	Failure	2	0.6	26	15.1	

AKI: Acute Kidney Injury; X^2: Chi square test.

TABLE 6: Demographic data between dead and discharged patients.

	Survivors (mean±sd) (%)	Non-survivors (mean±sd) (%)	p
Age (year)	58,5±18,5	66,6±15,3	0,000^{m}
Gender Female	153 46,4%	86 50 %	0,439^{X2}
Male	177 53,6%	86 50 %	
Height (cm)	165,1±9,9	163,4±10,1	0,076^{t}
Weight (kg)	76,1±18,5	84,2±17,3	0,030^{m}
Duration of stay (days)	6,4±9,1	15,5±15,3	0,000^{m}

m: Mann-Whitney U test; X^2: Chi square test; ^{t}: Independent samples t test.

TABLE 7: The comorbid diseases, APACHE II, SOFA, triceps thickness, waist circumference, urea, creatinin, prealbumin, albumin, $HC0_3$ and cholesterol measurements of survivors and non-survivors

		Survivors (mean±sd) (n-%)	Non-survivors (mean±sd) (n-%)	p
Comorbid diseases	None	250 75,8%	107 62,2%	0,001[X²]
	DM	9 2,7%	2 1,2%	
	HT	35 10,6%	27 15,7%	
	Stroke	8 2,4%	10 5,8%	
	Other	28 8,4%	26 15,1%	
APACHE II		12,5±7,2	28,0±6,8	0,000[m]
SOFA		4,0±3,1	9,7±3,2	0,000[m]
Triceps thickness (mm)		13,6±6,2	14,8±7,1	0,081[m]
Waist circumference (cm)		92,7±14,9	97,6±18,1	0,001[m]
Urea (mg/dl)		52,5±99,2	104,5±72,5	0,000[m]
Creatinine (mg/dl)		0,9±0,5	1,5±1,0	0,000[m]
Prealbumin (mg/dl)		15,8±6,7	10,5±5,5	0,000[m]
Albumin (mg/dl)		3,1±0,7	2,7±0,7	0,000[t]
$HC0_3$ (mEq/L)		21,2±4,4	21,7±6,1	0,115[m]
Cholesterol (mg/dl)		129,2±38,8	122,1±41,4	0,032[m]

APACHE: Acute physiology and chronic health evaluation system; SOFA: Sequental organ failure assessment; [m]: Mann-Whitney U test; X^2: Chi square test; [t]: Independent samples t test; DM: Diabetes mellitus; HT: Hypertension.

the subgroups as 13.8% Risk, 12,4% Injury and 15,1 % as Failure. Another study reported the incidence for ARF as 40,3 % in trauma patients.[25] Cruz et al. made a study on 2164 patients and reported 10.8% for ARF.[26] The authors reported as follows 19% R, 35% I, and 46% F. In our study we found that the incidence of ARF was 39.2%. The sub-groups was 21.3% for R, 12.4% for I and 5.6% for F. The differences between different studies may be due to different patients and number of centers enrolled into studies.

In our study, we found that the age of the patients in AKI group was higher than non-AKI group. Park et al. reported no difference according to ages.[24] Krasnalhia et al. found that the mean age of the patients with acute renal failure was 32+1.9 and they found no difference on ages between AKI and non-AKI patients.[25]

The relationship between antropometric measurements and acute renal injury was reported by many researhers.[27-29] Kumar et al. made a study on 378 patients and found that obesity (BMI >40 kg/ m^2) had a high relationship with acute renal injury.[27] Another study made by Hyunju et al. reported that the renal functions go worser on patients with obesity.[28] Wang et al. also reported the same. In our study we also found that in the AKI group the mean weight of the patients were higher.[29]

Renal failure in intensive care units are usually not as primary disease, is evolving the existing secondary diseases or as a component of multiorgan disfunction syndrome. Park et al. reported that pulmonary diseases was the most disease in the renal failure patients.[24] After pulmonary diseases, malignancies and gastrointestinal diseases were seen. In our study the primer disease was neurological diseases, after that gastrointestinal diseases, pulmonary diseases and malignancies will come. The heterogenity of the patient groups may be the reason for these results.

Comorbid diseases leading to a worsening of the patients in cases of ARF in intensive care unit.

In PICARD study comorbid diseases accompanied to ARF was congestive heart failure 39%, chronic renal diseases 30%, diabetes mellitus 29% and 21% liver insufficiency.[30] Krasnalhia et al. studied on 129 trauma patients and demonstrated that 14.72% of the patients had chronic diseses.[25] The authors demonstrated that the chronic diseases as follows: 5.4% diabetes mellitus, 3.9% hypertension and 2.3% stroke. In our study we found that the incidence of chronic diseases was 28.9%. 2.2% of the patients has diabetes mellitus, 12.4% had hypertension, 3.6% had stroke and 10.8% had two or more chronic diseases. Also we found that the chronic diseases were seen more frequently in AKI patients than non-AKI patients. We think that chronic diseases can be one of the factors that facilitate the development of acute kidney failure.

The development of kidney failure in patients hospitalized in intensive care units, extend the duration of hospital stay and increased mortality significantly. Park et al. found that the duration of the stay in intensive care of patients developed kidney failure was 18.3±18 days and the authors also found that, the patients developed kidney failure stay in the ICU more than other patients time.[24] The elongation of the ARF patients in intensive care unit was also reported by another study.[7] Similar to these studies in our study we demonstrated that in AKI group the duration of intensive care stay was 14.6±14.6 days. The stay was longer than non-AKI group.

Park et al. found that the SOFA scores were higher in patients with acute renal failure.[24] Similar to this study we also found that the APACHE II and SOFA scores were higher in AKI group.

In our study we found that the albumin and prealbumin levels were lower and urea, creatinine and HCO_3^- levels were higher in AKI group. We found no difference on cholesterol levels between AKI and non-AKI groups. Similar to our results different studies reported that a decrease in the levels of albumin and prealbumin associated with an increase in morbidity and mortality in the literature.[31-33]

Some of the studies reported the relationship between the patients with renal insufficiency and higher morbidity and mortality. A serious relationship between low cholesterol and prealbumin levels and acute renal failure has also been identified.[21,33-36] In our study we found no statistically significant difference on cholesterol levels between AKI and non-AKI groups, but similar to literature we found a relationship with lower cholesterol level and mortality.

Numerous epidemiological studies that examined patients with chronic renal failure show an inverse relationship between mortality and low serum bicarbonate levels.[22,31,37,38] In a study made by Dennis et al., the authors found a relationship between high HCO_3 and cardiovascular mortality.[38] We found no statistically significance between HCO_3 levels and mortality, but we found that HCO_3 levels were higher in AKI group.

The main limitation of our study was firstly our study was conducted at a single center included mix cases and may not represents the other centers. The second limitation was we prohibited the use of more complex measurements of kidney function so time to progression of acute kidney injury may have been elongated.

In conclusion, we think that patients especially in intensive care units with high age, excessive weight, chronic diseases, high urea, creatinine, HCO_3^- levels, low cholesterol, albumine and prealbumine levels are prone to renal failure. Those patients should be carefully followed for renal failure.

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