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RESEARCH ARTICLE

Evaluation of acute kidney injury patients in intensive care unit and determining effects of hemodialysis on sepsis

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ABSTRACT

Aim: Sepsis-associated acute kidney injury (AKI) is a frequent complication of critically ill patients, and results need for renal replacement therapy (RRT). We aimed to investigate the difference in vital signs, hemodynamic parameters, and laboratory values after receiving RRT in the AKI patients with/without sepsis. Also, we examined the different renal injury grading systems relationships used in intensive care units (ICU).

Methods: RRT-treated patients due to AKI were enrolled. Patients were divided into two groups by using Sepsis-2 criteria (2012); whether there is sepsis or not. Acute physiology and chronic health evaluation II (APACHE II) scores, 28th and 90th day mortality recorded. RIFLE classes, renal sequential organ failure assessment (SOFA) scores, and kidney disease: improving global outcomes (KDIGO), stages were also calculated. Patients' Glasgow Coma Scale (GCS), vital parameters, laboratory values, Horowitz rates, vasopressor/inotropic agent requirements at RRT start, 12th and 24th hours were recorded.

Results: 153 patients were included in the study, and 93 were septic. APACHE II score and 28th day mortality were significantly higher in Group Sepsis. Advanced age was found to be associated with 90th day mortality. Both in two groups many parameters such as acidosis, Horowitz ratio, and GCS improved after RRT initiation. When renal scoring systems were compared with each other KDIGO was associated with the RIFLE classification and renal SOFA.

Conclusion: Many improvements were observed in all AKI patients after RRT but in septic patients, oxygenation and GCS showed better improvement. The mortality rate increased when AKI got complicated with sepsis.

Keywords: acute kidney injury, intensive care medicine, renal replacement therapy, sepsis

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INTRODUCTION

Deterioration in renal functions has been named in different ways. Acute kidney injury (AKI) is characterized by decline in the glomerular filtration rate (GFR), elevation of serum blood urea nitrogen (BUN), creatinine, and other metabolic waste products. The term AKI rather than acute renal failure (ARF), is highly used because of not every case results with organ failure (1).

Sepsis-associated acute kidney injury (S-AKI) is a frequent complication of the critically ill patient and is associated with high morbidity and mortality. Nearly 1 in 3 patients with sepsis develop AKI so the global incidence of S-AKI might be approximately 6 million cases or nearly 1 per 1000 population (1,2).

There has been made a variety of definitions to standardize the diagnosis of AKI. In 2004 Acute Dialysis Quality Initiative (ADQI) Group made the RIFLE classification to be used in the diagnosis and treatment of AKI. In 2007, the RIFLE criteria have been revised and corrections were made by the Acute Kidney Injury Network (AKIN) Group (3). In March 2012 KDIGO (Using the Kidney Disease: Improving Global Outcomes), the new staging system is developed for the diagnosis of AKI based on RIFLE and AKIN criteria (4). In KDIGO, AKI severity is divided into three phases shown in Figure 1.

The first treatment choice in AKI patients is supportive, in serious renal injury cases this means RRT. In a study the incidence of patients diagnosed AKI requiring RRT is 11 of 100,000 people per year (5).

There are many studies in the literature examining the relationship between AKI and sepsis in intensive care units (ICUs) (3,4,6). However, there are not enough studies evaluating the AKI patients receiving RRT comparing groups with and without sepsis and the effectiveness of RRT in septic patients. In our study, we aimed to investigate the difference in hemodynamic parameters and laboratory values after receiving RRT in the AKI patients with or without sepsis. Also, we wanted to display the differences in mortality rates and examine the different renal injury grading systems relationships used in intensive care patients.

MATERIALS AND METHODS

After obtaining ethical approval from Uludağ University Faculty of Medicine, Health Application and Research Center on 9 December 2014 (2014-23/13), CVVHD (Continuous veno-venous hemodialysis)

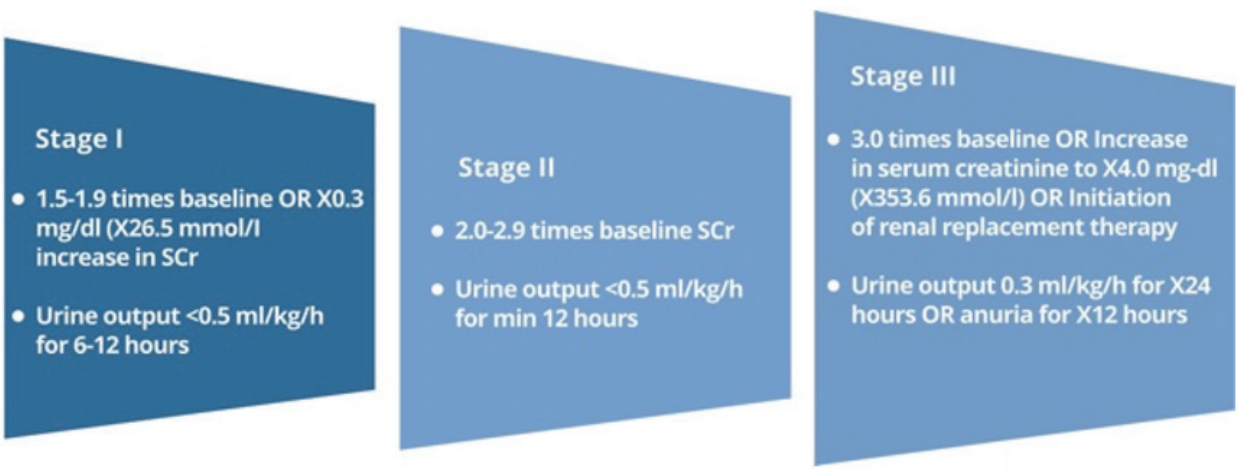

Figure 1. KDIGO stages.

SCr: Serum creatinine value.

treated patients due to the ARF who were accepted to the Reanimation Unit between 01.01.2010–30.06.2014 were enrolled. Patients' demographic datas, concomitant systemic diseases and laboratory values were analyzed retrospectively on the electronic archive of Uludağ University School of Medicine.

A total of 294 patients data were analyzed. 141 patients were excluded; 90 patients were already diagnosed chronic renal failure (CRF), 1 case was 23 weeks pregnant, 26 cases died within 24 hours of CVVHD, 3 patients were under 18 years old, 20 cases had lack of data, 1 case transferred to another clinic within 24 hours CVVHD. A total of 153 patients were enrolled in the study.

Patient demographics, APACHE II (Acute Physiology and Chronic Health Evaluation II) scores, ICU admission indication, 30th day and 90th day mortality were recorded. RIFLE classes, renal SOFA scores, and KDIGO stages were calculated at the beginning of CVVHD. Patients Glasgow coma score (GCS), systolic and diastolic arterial pressure, heart rate, body temperature, central venous pressure, mechanical ventilation and oxygenation parameters, laboratory values, analysis of arterial blood gases, Horowitz rates, vasopressor or inotropic agents requirements in CVVHD start, the next 12 and 24 hours were recorded. GFR (glomerular filtration rate) was calculated by the 'Modification of Diet in Renal Disease' (MDRD) formula. After the decision to start dialysis, it was performed using a Fresenius Medical Care Multifiltrat device with ULTRAFLUX AV600S 1,4m² membrane.

Statistical analysis of the data was held by Uludağ University School of Medicine Department of Biostatistics, at the IBM SPSS (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.) statistical software. Data show normal distribution were analyzed with the Shapiro-Wilk test. The comparison of the two independent groups, the Mann-Whitney U test for continuous data, and the comparison of the two groups dependent Wilcoxon signed rank tests were used. The level of significance was set at p=0.05.

RESULTS

A total of 153 patients were included in the study. There were 93 patients with septic shock (Group S) and 60 patients without septic shock (Group C). Demographic data of the patients, admission APACHE II scores and concomitant systemic diseases were reported in Table 1. APACHE II score was significantly higher in Group S (p <0.001).

Table 1. Demographic data and accompanying systemic disease of patients (mean ± SD)

	Group C (n=60)	Group S (n=93)	p value
Age	54.3 (18.3)	57.7 (16.3)	0.239
Gender (F/M)	25/35	32/61	0.365
APACHE II score	18.8 (±6.8)	24.5 (±7.4)	<0.001
Concomitant disease			
Hypertension	22 (36.7)	35 (37.6)	0.904
Diabetes mellitus	11 (18.3)	27 (29)	0.192
Malignancy	8 (13.3)	20 (21.5)	0.288
Cardiac failure	13 (21.7)	33 (35.5)	0.101

F: Female, M: Male, APACHE II: Acute Physiology and Chronic Health Evaluation.

Table 2. Laboratory values and vital parameters for Group C [median (min-max)]

	Initiation	12th hour	24th hour	p-value Initiation-12th hour	p-value Initiation-24th hour
GCS	7 (3-11)	7 (3-11)	7 (3-11)	0.401	0.004
MAP (mmHg)	76 (52-134)	76 (50-128)	77 (39-118)	0.717	0.843
Urea (mg/dL)	175 (31-382)	141 (24-340)	117 (30-294)	0.001	<0.001
Creatinine (mg/dL)	3.3 (1-10)	2.55 (0.5-8)	2.05 (0.5-5.7)	0.001	<0.001
GFR (mL/min/1.73 m²)	88 (24-348)	118 (32-751)	148 (50-957)	<0.001	<0.001
pH	7.31 (7.11-7.5)	7.35 (7.12-7.5)	7.36 (7.07-7.5)	0.012	0.002
Bicarbonate (mmol/L)	20 (11-42)	21 (14-31)	22 (11-40)	0.289	0.069
Lactate (mg/dL)	17.5 (5-166)	18 (5-140)	17 (6-141)	0.147	0.118
SpO_2 (%)	98 (81-100)	98 (87-100)	98 (84-100)	0.336	0.855
FiO_2 (%)	0.8 (0.3-1)	0.8 (0.3-1)	0.5 (0.3-1)	<0.001	<0.001
PEEP (cm H_2O)	7 (5-15)	7 (4-15)	6 (4-13)	0.119	<0.001
Body temperature (°C)	36.9 (35-39)	36.5 (36-35)	36.9 (35.7-39.2)	0.051	0.601

GCS: Glasgow Coma Score, MAP: Mean arterial pressure, GFR: Glomerular filtration rate, SpO_2: Pulse oximeter, FiO_2: Fraction of inspired oxygen, PEEP: Positive end-expiratory pressure.

Table 3. Laboratory values and vital parameters for Group S [median (min-max)]

	Initiation	12th hour	24th hour	p-value Initiation-12th hour	p-value Initiation-24th hour
GCS	6 (3-11)	7 (3-11)	7 (3-11)	0.005	0.001
MAP (mmHg)	71 (42-108)	73 (40-106)	70 (32-107)	0.472	0.422
Urea (mg/dL)	155 (22-314)	124 (22-298)	97 (14-273)	<0.001	<0.001
Creatinine (mg/dL)	3 (0.3-8.4)	2.7 (0.5-7)	2.2 (0.5-7)	<0.001	<0.001
GFR (mL/min/1.73 m²)	103 (33-1319)	129 (38-680)	161 (30-1002)	<0.001	<0.001
pH	7.32 (6.9-7.6)	7.35 (7-7.53)	7.37 (7-7.54)	0.003	<0.001
Bicarbonate (mmol/L)	20 (10-32)	21 (14-35)	21 (13-53)	0.004	0.002
Lactat (mg/dL)	18 (3-164)	18 (7-143)	17 (6-152)	0.701	0.121
SpO_2 (%)	97 (75-100)	98 (68-100)	97 (70-100)	<0.001	0.031
FiO_2 (%)	0.65 (0.3-1)	0.55 (0.25-1)	0.5 (0.25-1)	<0.001	<0.001
PEEP (cm H_2O)	7 (4-15)	7 (4-15)	7 (4-14)	0.002	<0.001
Body temperature (°C)	37.3 (35.5-39.5)	36.8 (34.8-39.4)	36.9 (35.7-39.2)	<0.001	0.003

GCS: Glasgow Coma Score, MAP: Mean arterial pressure, GFR: Glomerular filtration rate, SpO_2: Pulse oximeter, FiO_2: Fraction of inspired oxygen, PEEP: Positive end-expiratory pressure.

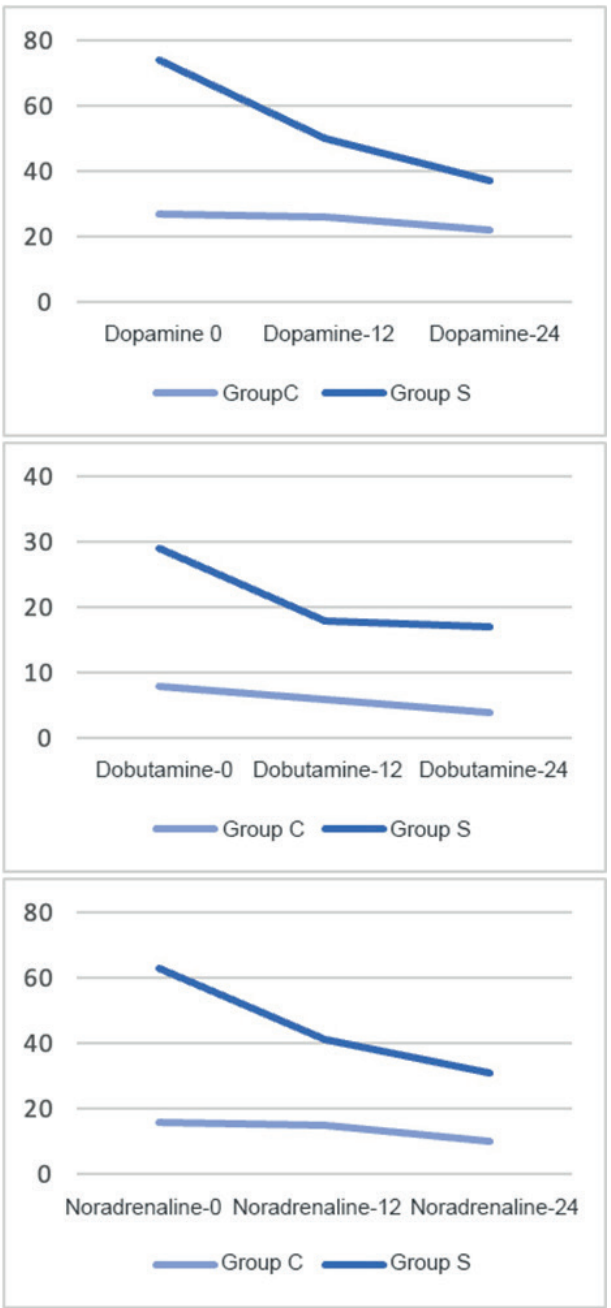

Figure 2. Inotropic and vasopressor drug use.

There were no significant differences between the two groups' KDIGO stages, RIFLE classification and renal SOFA scores in CVVHD start. When renal scoring systems were compared with each other, KDIGO was associated with the RIFLE classification and renal SOFA. Significance values were p<0.001 r=0.354; r=0.248 p=0.02.

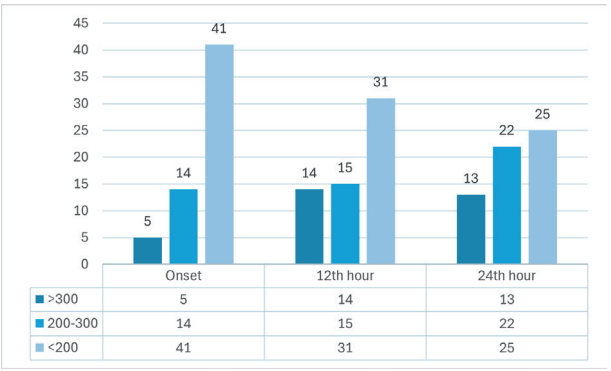

Figure 3. Horowitz ratio of Group C (n).

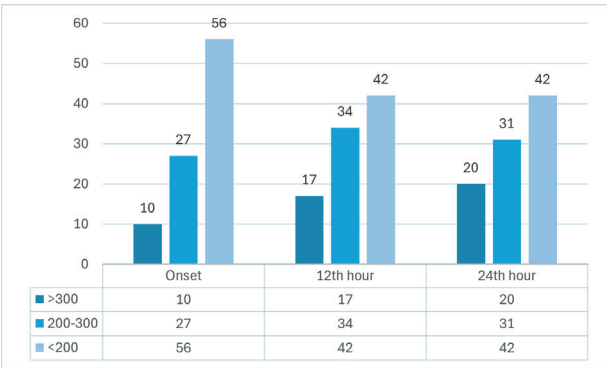

Figure 4. Horowitz ratio of Group S (n).

When age of the patients and 28-90th day mortality relationship are compared; advanced age increases the incidence of mortality at day 90 (p=0.002).

The comparison of laboratory values and vital parameters between CVVHD start the day, 12 and 24 hours after the treatment of Group C and Group S are shown in Table 2 and Table 3.

The comparison of inotropic and vasopressor agent use is shown in Figure 2. In both groups, the use of inotropic and vasopressor agents decreased significantly at 12 and 24 hours after CVVHD (p<0.001).

Horowitz ratio significantly increased after CVVHD in both groups. The significance value is p<0.001 in both groups in 12th hour, while 24th hour for Groups C's significance is p=0.04 and Groups S's significance is p=0.05. Changes are shown in Figure 3 and Figure 4.

DISCUSSION

Acute kidney injury is a clinical syndrome that accompanied by usually reversible reduction in GFR, accumulation of nitrogen metabolites such as urea and creatinine, fluid and electrolyte imbalances, and acid-base metabolism disorders which is closely associated with high mortality.

The incidence of AKI is increased in elderly patients. In our study, although there was no difference in mean age between Group C and Group S, advanced age was associated with 90th day mortality.

Different factors may play a role in the etiology of AKI. One of the most common causes of AKI in the ICU is sepsis. In Poston and Koyner's (2019) study; sepsis is associated with up to 50% of AKI, and up to 60% of patients with sepsis have AKI (7). In Parmar et al.'s (2009) study, more than 50% of AKI patients were in sepsis or septic shock (8). In our study, 60% of patients with AKI were in septic shock.

The presence of systemic diseases increase the risk of developing AKI. In our study, 2% of patients had diabetes mellitus, 37% had hypertension, and 18% had different malignancies.

The presence of AKI significantly increases mortality in intensive care, mortality rate rises to 90% in cases requiring RRT (7). In Parmar et al's retrospective study (2009) including 211 septic patients; 28th day mortality was found to be significantly higher in the AKI group (8). In another study performed in sepsis patients, AKI has been shown to increase the 28th day mortality (9). Our study supports previous studies; 28th day mortality rate is 66% in Group S which is significantly higher than Group C, while the 90th day mortality rate is 56%.

Many different scoring systems have been developed to detect the severity of the clinical condition of patients in the ICU. These scoring systems are important because they show a direct relationship with mortality rates. Using a combination of different scores allow better prediction about patients. One of the previous studies showed that AKI patients had a higher APACHE II score. In the same study, the relationship with the AKIN classification and KDIGO was investigated, and they were found to be highly correlated (9). We also found a significantly higher APACHE II value in Group S than in Group C. In our study, KDIGO staging was associated with RIFLE classification and renal SOFA score.

Poukkanen et al. (2013) conducted a multicenter FINNAKI study; patients' KDIGO stages were calculated during their stay in the ICU and worst values were included in the study (10). Only KDIGO stage 3 was found to be associated with 90th day mortality. In another study, patients' RIFLE classification and KDIGO stages were calculated on admission to ICU, and no relationship was observed (11). In our study, patients' KDIGO stages, RIFLE classifications, and renal SOFA scores were calculated only on the day CVVHD started, and were not associated with either 28th day or 90th day mortality. We believe that this is because the staging of patients in our study and the calculation of scores were only made on the day CVVHD started, and recorded values are inadequate to determine the relationship between mortality.

In shock status, the use of inotropic and vasopressor agents to provide appropriate mean arterial pressure becomes necessary. Legrand et al. (2013) examined the use of inotropic and vasopressor agents between septic patients with or without AKI and found no significant difference (12). Abdo et al. (2012) published an 18-case series with MODS, after CVVHD was compared to non-septics needs of noradrenaline in the septic group had an overall reduction 12th hour (13). In our study, the use of a vasopressor and inotropic agent at the initiation of RRT was 47% in Group C and 87% in Group S. In both groups, the use of these agents decreased in 12th and 24th hour. When a comparison was made between the groups at 24th hour, decrease was more significant in Group S. In septic patients' plasma levels of many inflammatory cytokines are elevated and also when local inflammation in kidney is added too; risk of developing AKI gets higher. Another result of inflammatory cytokines is cardiac depression and decreased systemic vascular resistance. In a study performed in neonates with septic shock, normal blood pressure values could be maintained after 12-hour CVVHD (14). This also can be the explanation for our findings.

One of the changes reported in the MODS case series was the improvement in serum bicarbonate values of the septic group (13). Another study targeted further improvement with dialysis in septic patients; however, there were no significant changes in pH and lactate values. In our study, the pH increased in both groups. There were no significant changes in lactate levels in both groups, it was only a significant increase in the bicarbonate value of Group S at12th and 24th hours.

Many different methods can be used to monitor the level of consciousness. One of the most commonly used methods in clinical practice is GCS. Bagshaw's study showed no difference in GCS after CVVHD (9). In our study, there was no difference in the initial GCS scores between the groups. While there was a significant change in Group C only at 24th hour, in Group S recovery started at 12th and continued at 24th hour.

As a result of the CVVHD expected, nitrogen plasma metabolites reduced. A significant reduction in nitrogen plasma metabolites was detected in all patients. In addition, both groups also showed significant decrease in oxygen demand and increase in Horowitz ratio, in addition to Group S, 12th and 24th hour pulse oximetry values increased. The reduction in renal uremia improved respiratory system, seems to confirm the relationship between the lung and the kidney. Also, more inflammation injury characterized in Group S showed more improvement in respiratory parameters after CVVHD, supporting that the injury in the lungs dose not only depend on the volume overload also are as a result of inflammation.

Acknowledgements

This study had several limitations. First, it wasn't built as a multicenter study, it was performed in our hospital. Also, sepsis related biomarkers were not measured from blood samples, and changes in their levels after RRT couldn't show numerical. The follow-up period in this study was short, and the association between sepsis and long-term acute kidney failure did not followed up on. In conclusion, improvement observed in many parameters in all AKI patients after CVVHD application; however, in septic patients, oxygenation and GCS showed better improvement. The mortality rate increased when AKI got complicated by sepsis. KDIGO, another renal injury grading system, was found to correlate with RIFLE criteria and renal SOFA scores.

Ethical approval

This study has been approved by the Faculty of Medicine, Uludağ University Ethics Committee (approval date 09/12/2014, number 2014-23/13). Written informed consent was obtained from the participants.

Author contribution

Concept: İA; Design: İA, FŞK; Data Collection or Processing: İA, EIS; Analysis or Interpretation: İA; Literature Search: İA; Writing: İA. All authors reviewed the results and approved the final version of the article.

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The authors declare the study received no funding.

Conflict of interest

The authors declare that there is no conflict of interest.

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