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Clinical characteristics and short-term outcome of dialysis-requiring acute kidney injury in critically ill patients

Kritik hastalarda diyaliz gerektiren akut böbrek yetmezliğinin klinik özellikleri ve kısa dönemli sonuçları

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Abstract

Aim: Dialysis-requiring acute kidney injury (D-AKI) in intensive care unit (ICU) continues to be associated with adverse outcomes of high mortality and dialysis-dependent chronic kidney disease (CKD). This retrospective study aimed to identify clinical characteristics of dialysis-requiring AKI and renal replacement therapy (RRT) which replaces the normal blood-filtering function of the kidneys in current ICU practice.

Methods: This retrospective cohort study was conducted in a 20-bed, third level ICU of a University Hospital between 2011 and 2017. In total, 145 D-AKI patients who underwent RRT were identified. Hospital records of patients with D-AKI were retrospectively analyzed for demographics, medical history, clinical characteristics, details of RRT modality, and short-term outcome.

Results: Of the 1689 patients investigated, 145 had D-AKI. The median age of the patients included in the study was 73 years. Septic etiology was the most common suspected cause for D-AKI development. Fifty-two patients (35.9%) underwent continuous RRT (CRRT) while intermittent hemodialysis was used in 93 patients (64.1%). Mechanical ventilation and inotropic support were more commonly used in CRRT patients than IHD patients (P=0.03). In total, in-hospital mortality rate was 73.1% while rate of dialysis-dependent CKD on discharge was 6.2%. Mortality rate was significantly higher in CRRT (84.6%) patients than in IHD patients (66.7%, P=0.019).

Conclusion: Our study results reveal that sepsis appears to be the most important cause of D-AKI in intensive care patients. D-AKI was observed more frequently in elderly patients and associated with an increased risk of short-term mortality.

Keywords: Critically ill patients, Acute kidney injury, Dialysis, Continuous renal replacement therapy, Intermittent hemodialysis

Öz

Amaç: Diyaliz gerektiren akut böbrek hasarı yoğun bakım ünitelerinde yüksek mortalite ve diyalize bağımlı kronik böbrek hastalığı gibi olumsuz sonuçları ile ilişkilidir. Bu retrospektif çalışma günümüz yoğun bakım pratiğinde diyaliz gerektiren akut böbrek hasarının klinik özelliklerini ve renal replasman tedavi yöntemlerini tanımlamayı amaçlamıştır.

Yöntemler: Bu retrospektif kohort çalışma, bir üniversite hastanesinin 20 yataklı üçüncü basamak yoğun bakım ünitesinde 2011-2017 arasında gerçekleştirilmiştir. Toplamda, renal replasman tedavisi uygulanan 145 diyaliz gerektiren akut böbrek hasarı hastası tanımlanmıştır. Diyaliz gerektiren akut böbrek hasarı hastalarının hastane kayıtları demografi, tıbbi öykü, klinik özellikler, renal replasman tedavisi detayları ve ısa dönemli sonuçlar için retrospektif olarak analiz edilmiştir.

Bulgular: İncelenen 1689 hastanın 145'inde diyaliz gerektiren akut böbrek hasarı mevcuttu. Dahil edilen hastaların ortanca yaşı 73 idi. septik etiyoloji, diyaliz gerektiren akut böbrek hasarı gelişiminde en sık şüphelenilen nedendi. Elli iki hasta (%35,9) sürekli renal replasman tedavisi hastaya uygulanmışken 93 hastaya (%64,1) aralıklı hemodiyaliz uygulanmıştır. Sürekli renal replasman tedavisi uygulanan hastalarda mekanik ventilasyon ve inotrop desteği daha sık kullanılmıştır (P=0,03). Toplamda, hastane içi mortalite oranı %73,1 iken taburculukta diyaliz bağımlı kronik böbrek hastalığı oranı %6,2 idi. mortalite oranı sürekli renal replasman tedavisi uygulanan hastalarda anlamlı olarak daha yüksekti (%84,6'ya karşılık %66,7, P=0,019).

Sonuç: Çalışmamızın bulguları yoğun bakım hastalarında diyaliz gerektiren akut böbrek hasarının en önemli nedeninin sepsis olduğunu göstermektedir. Diyaliz gerektiren akut böbrek hasarı yaşlı hastalarda daha fazla görülmüştür ve kısa dönemli mortalite riskinde artış ile ilişkilidir.

Anahtar kelimeler: Kritik hasta, Akut böbrek hasarı, Diyaliz, Sürekli renal replasman tedavisi, Aralıklı hemodiyaliz

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Introduction

Acute kidney injury (AKI) is a common and serious problem of intensive care unit (ICU) patients, related with high in-hospital mortality rates and dialysis-dependent chronic kidney disease [1-4]. Advanced age, increased AKI severity, dialysis requirement, infections or sepsis, oliguria, number of failing organs, mechanical ventilation requirement and cardiovascular failure are associated with increased mortality of AKI patients in the ICU [1,5-8]. Management of AKI is variable and includes renal replacement therapy (RRT) with hemodialysis (HD) [9]. While intermittent HD (IHD) continues to be in use, continuous veno-venous HD or continuous RRT (CRRT) has been increasingly adapted since 2000, mostly in ICU setting [10].

We aimed to determine the demographic and clinical characteristics, dialysis modalities (IHD or CRRT), and short-term outcomes of dialysis-requiring AKI (D-AKI) patients in a tertiary hospital ICU within routine medical practice for providing exploratory epidemiological evidence. The secondary aim was to compare IHD and CRRT modalities in terms of patient populations and outcomes in routine ICU practice.

Materials and methods

This study protocol was conducted in accordance with principles of Declaration of Helsinki and good clinical practice. In this observational retrospective study, consecutive adult (≥18 years) patients who were admitted to the third level, 20-bed ICU of a University Hospital with D-AKI were included. Patients who underwent kidney transplantation, those requiring chronic dialysis before ICU admission, and patients with incomplete medical records were excluded from the study.

AKI was determined with KDIGO criteria [11]. By definition of the study population, all patients had KDIGO stage 3 AKI. D-AKI was defined as acute dialysis in patients without previously registered end-stage renal disease [10]. Patient records between 2011-2017 were searched, and those with AKI who underwent RRT and stayed in the ICU for more than 24 hours were noted. Electronic data codes, keywords and matching records were obtained. All patient-level data were obtained and analyzed without personally identifying information. Variables of age, sex, comorbidities, indications for ICU admittance and primary suspected cause of AKI, Acute Physiology and Chronic Health Evaluation (APACHE II) Score calculated within 24 hours of ICU admission [12], vasopressor requirement and mechanical ventilation use at the beginning of dialysis, length of stay (LOS) in ICU and hospital, in-hospital mortality, and HD requirement for kidney failure following discharge (i.e. stage 5 chronic kidney disease as defined by Kidney Disease: Improving Global Outcomes [KDIGO]) [13] were recorded. Charlson Comorbidity Index (CCI) score [14] was calculated with age and comorbidity history of patients and classified as low (0-1) or high (≥2). Values of laboratory parameters for hemoglobin, serum albumin, creatinine, blood urea nitrogen (BUN), and glomerular filtration rate (calculated with Modification of Diet in Renal Disease formula) [15] first obtained at initial hospital admission and before the first HD session were also noted.

Patients were classified according to RRT type employed for the treatment of AKI into two groups as IHD and CRRT to compare baseline characteristics and outcomes.

RRT was performed solely as IHD or CRRT, a decision taken by nephrologists and ICU attending physicians considering the hemodynamic stability of the patient. IHD was performed within 3 to 5 hours with AKI 96 dialysis machine (Gambro Lundia AB, Sweden) with bicarbonate-based dialysate and polysulfone hollow-fiber dialyzer (F8 High Performance Steam, Fresenius Medical Care, Germany). CRRT was administered with Prismaflex System (Baxter, IL, United States) as continuous veno-venous hemofiltration with bicarbonate-based dialysate, saline-based replacement fluid, and AN 69 dialyzer membrane. All HD modalities were performed through a venous access dialysis catheter using the anticoagulant agent of heparin.

Statistical analysis

Demographical and clinical characteristics were presented as number (%) or median (range). Non-parametrical statistical tests of Mann-Whitney U and Pearson χ^2 or Fisher's exact tests were used for continuous and categorical variables, respectively, for comparisons between IHD and CRRT groups. Data analysis was carried out with IBM SPSS Statistics (version 20; IBMCorp., Armonk, NewYork) software. A two-sided *P*-value of <0.05 was regarded as significant.

Results

A total of 1689 patients were screened within a seven-year period and 145 patients with the diagnosis of D-AKI and complete medical records were found. IHD was used in 93 patients (64.1%) whereas CRRT was used in 52 (35.9%). Median age was 73 (20-93) years with male population predominance (55.9%). Based upon their medical history, 118 patients (81.4%) (79 IHD patients [84.9%] and 39 CRRT patients [75.0%]) had comorbidities. Age, gender, CCI categories, and selected comorbidities of the patients were similar between IHD and CRRT groups except for coronary artery disease (28.0% vs 13.5%, respectively; *P*=0.046). A surgical indication for ICU admission was found in 52 patients (35.9), mostly as postoperative need for follow-up in an ICU setting (n=44, 84.6%). Respiratory failure was the most common overall cause for ICU requirement (n=56, 38.6%). Prevalence of selected indications for ICU admission and median APACHE II scores were similar between IHD and CRRT patients. CRRT patients had higher vasopressor (94.2% vs. 81.7%) and mechanical ventilation (100% vs. 91.4%) needs than IHD patients at the beginning of dialysis (*P*=0.036 and 0.030, respectively). Septic etiology was the most common cause (57.9%) in the patient population who developed D-AKI. In addition, the number of patients with septic etiology in the CRRT group was higher than in the IHD group (71.2% vs. 50.5%, *P*=0.053). Detailed demographical and clinical patient characteristics are presented in Table 1.

Diagnostic laboratory values of blood parameters are presented in Table 2. CRRT group had lower median BUN and higher median GFR than in the IHD group at hospital admission (46 vs 50 mg/dL and 65.5 vs 57.0 mL/min/1.73 m^2, respectively; *P*=0.046 for both). Prior to initiation of HD, CRRT patients had lower median creatinine (2.4 vs 3.3 mg/dL) and BUN (120.5 vs

144 mg/dL) levels and higher median GFR (25.5 vs 18 mL/min/1.73 m^2; P=0.003 for all) than those in the IHD group.

Among the patient population of D-AKI, median LOS in the ICU and hospital were 17 and 22 days, respectively. LOS in the ICU and hospital were longer in IHD group (20 vs 9.5 days and 26 vs 18.5 days, respectively; P=0.008 for both). In-hospital mortality rate was 73.1% for all patients. Mortality rate was higher in CRRT patients (84.6 vs 66.7%, P=0.019) while dialysis-requiring kidney failure rates at discharge were similar, albeit the patient numbers were small (Table 3).

Table 1: Clinical and demographical characteristics of patients admitted to intensive care unit with dialysis-requiring acute kidney injury

Characteristic	All patients (n=145)	Hemodialysis modality IHD (n=93)	CRRT (n=52)	*P*-value
Median age (years), (range)	73 (20-93)	74 (20-93)	71 (26-89)	0.095
Sex, No. (%)				
Female	64 (44.1)	45 (48.4)	19 (36.5)	0.168
Male	81 (55.9)	48 (51.6)	33 (63.5)	
Charlson comorbidity index, No. (%)				
Low (0-1)	22 (15.2)	11 (11.8)	11 (21.2)	0.133
High (≥2)	123 (84.8)	82 (88.2)	41 (78.8)	
Selected comorbidities, No. (%)				
Hypertension	80 (55.2)	56 (60.2)	24 (46.2)	0.102
Coronary artery disease	33 (22.8)	26 (28.0)	7 (13.5)	0.046
Atrial fibrillation	9 (6.2)	5 (5.4)	4 (7.7)	0.722b
Chronic heart failure	19 (13.1)	14 (15.1)	5 (9.6)	0.352
Diabetes	37 (25.5)	28 (30.1)	9 (17.3)	0.090
Chronic obstructive pulmonary disease	19 (13.1)	11 (11.8)	8 (15.4)	0.543
Dementia	13 (9.0)	9 (9.7)	4 (7.7)	0.771b
Cerebrovascular disease	17 (11.7)	13 (14.0)	4 (7.7)	0.296b
Other	22 (15.2)	9 (9.7)	9 (17.3)	NA
Primary indication type, No. (%)				
Medical	93 (64.1)	62 (66.7)	31 (59.6)	0.396
Surgical	52 (35.9)	31 (33.3)	21 (40.4)	
Selected primary indication for ICU admission, No. (%)				
Respiratory failure	56 (38.6)	36 (38.7)	20 (38.5)	0.97
Postoperative admission	44 (30.3)	28 (30.1)	16 (30.8)	0.934
Sepsis	14 (9.7)	8 (8.6)	6 (11.5)	0.566
Other	31 (21.4)	21 (22.6)	10 (19.2)	NA
Median APACHE II score, (range)	30 (11-48)	29 (11-48)	33 (16-48)	0.134
Vasopressor need, No. (%)	125 (86.2)	76 (81.7)	49 (94.2)	0.036
Mechanical ventilation use, No. (%)	136 (93.8)	85 (91.4)	52 (100.0)	0.030
Suspected primary cause for AKI				
Septic	84 (57.9)	47 (50.5)	37 (71.2)	0.053
Cardiovascular	54 (37.2)	41 (44.1)	13 (25.0)	
Other	7 (4.8)	5 (5.4)	2 (3.8)	

a: 93 patients (64.1%) (65 IHD [69.9%] and 28 CRRT [53.8%] patients) had more than one comorbidity, b: Fisher's exact test was used, AKI: acute kidney injury, APACHE II: acute physiology and chronic health evaluation, CRRT: Continuous renal replacement therapy, ICU: intensive care unit, IHD: intermittent hemodialysis, NA: not applicable.

Table 2: Values of blood diagnostics of patients at hospital admission and prior to hemodialysis initiation in intensive care unit

Parameter, Median (range)	All patients (n=145)	Hemodialysis modality IHD (n=93)	CRRT (n=52)	*P*-value
Creatinine (mg/dL)				
At admission	1.1 (0.4-2.6)	1.2 (0.4-2.6)	1.1 (0.6-2.1)	0.239
Before hemodialysis	3.0 (1.0-8.0)	3.3 (1.0-8.0)	2.4 (1.0-8.0)	0.013
Blood urea nitrogen (mg/dL)				
At admission	48 (13-160)	50 (16-160)	46 (13-94)	0.017
Before hemodialysis	138 (34-342)	144 (35-342)	120.5 (34-279)	0.015
Glomerular filtration rate (mL/min/1.73 m2)				
At admission	59 (26-124)	57 (31-121)	65.5 (26-124)	0.046
Before hemodialysis	19 (6-89)	18 (8-66)	25.5 (6-89)	0.003
Albumin (g/dL)				
At admission	3.2 (2.0-4.8)	3.2 (2.0-4.7)	3.3 (2.1-4.8)	0.475
Before hemodialysis	2.5 (1.0-4.0)	2.5 (1.6-4.0)	2.5 (1.0-3.6)	0.341
Hemoglobin (g/dL)				
At admission	11.0 (7.1-18.0)	11.0 (7.7-18.0)	12.0 (7.1-17.0)	0.071
Before hemodialysis	8.0 (7.0-16.0)	8.0 (7.0-15.0)	8.0 (7.0-16.0)	0.682

CRRT: Continuous renal replacement therapy, IHD: intermittent hemodialysis

Table 3: Length of stays and clinical outcomes of dialysis-requiring acute kidney injury patients

Parameter	All patients (n=145)	Hemodialysis modality IHD (n=93)	CRRT (n=52)	*P*-value
Median LOS in ICU (days), (range)	17 (2-156)	20 (2-156)	9.5 (2-154)	0.001
Median total LOS in hospital (days), (range)	22 (2-157)	26 (2-157)	18.5 (2-154)	0.008
In-hospital mortality, n (%)	106 (73.1)	62 (66.7)	44 (84.6)	0.019
Chronic RRT need on discharge, n (%)	9 (6.2)	8 (8.6)	1 (1.9)	0.157

CRRT: Continuous renal replacement therapy, ICU: intensive care unit, IHD: intermittent hemodialysis, LOS: length of stay, RRT: renal replacement therapy

Discussion

This study was conducted to determine factors associated with D-AKI patients followed up in a single-institution ICU. Our study population comprised of patients with advanced age (median age over 70 years), high burden of comorbidities, and high proportion of septic etiology for D-AKI along with extensive need for ventilator and vasopressor support. Therefore IHD was the preferred method of RRT in two-thirds of the patients. Sepsis was present in less than ten percent of the patients at ICU admission whereas over the course of ICU stay, D-AKI developed due to septic etiologies in over half of the patients. This finding indicates the importance of prevention of hospital-acquired infections in critically ill patients. Given our patient population with these high-risk AKI characteristics, observed in-hospital mortality in nearly three-quarters of the overall study population was considered to be in line with previous studies [1,16,17]. Hoste et al. [9] reported a median age of 65 in their AKI cohort with sepsis and hypovolemia being the most common etiologies for AKI development. About half of their AKI patients had KDIGO stage 3 disease, which was significantly associated with increased risk of mortality when compared with the group without AKI. Majority (75%) of RRT sessions were reported to have been conducted with CRRT, yet association of RRT modalities with mortality was not analyzed in their study [1]. Wilson et al. reported significantly increased in-hospital mortality (64%) in D-AKI group when compared with AKI patients who did not require RRT (22%) [16]. AKI was classified with Acute Kidney Injury Network staging system in their study [16]. In the extension phase of a randomized trial for RRT intensity for AKI, Gallagher et al. [17] reported around 60% of mortality with long-term follow-up. Increasing age was found to be predictive of increasing mortality.

While rates of mortality and/or chronic kidney failure associated with an in-hospital episode of AKI decreased over the years [18-21], critically ill patients with high risk factors and dialysis-requiring AKI continue to have a poor prognosis. A subgroup of AKI patients (6%) were discharged with a diagnosis of dialysis-requiring chronic kidney disease in our patient cohort, an expected outcome after AKI with a frequency increasing with AKI severity [22,23]. Depending on the patient cohort and duration of follow-up, crude rates of chronic kidney failure or end-stage renal disease development following AKI range from 1% to 8% [2,17,18,24-26].

Baseline clinical characteristics and outcomes of our patients differed according to the RRT modality of choice. Significantly higher numbers of CRRT patients had a need for mechanical ventilation and vasopressor support with a trend for higher number of patients with a suspected septic cause for AKI development. Additionally, CRRT patients had a higher in-hospital mortality rate when compared to the IHD group. An earlier observational study with relatively younger AKI patients who underwent RRT in the ICU also noted higher diagnosis of sepsis, use of mechanical ventilation and inotropic agents, and in-hospital mortality rates among CRRT patients compared to the IHD group, although probability of survival at 12 months were similar between these groups [27].

Requirement for mechanical ventilation [5,28], vasopressors [28], and acute cardiovascular failure [6] have been

associated with increased mortality in AKI patients. KDIGO guidelines recommend CRRT as the modality of RRT choice in hemodynamic instability, based mostly on theoretical advantage for better fluid balance control and circumstantial evidence of improvement of cardiovascular parameters [14]. While randomized controlled trials comparing IHD and CRRT in AKI consistently found no difference for survival outcomes [29,30], these trials largely excluded patients with severe illness and hemodynamic instability and involved crossover between RRT modalities [14,31]. Therefore, causal relation between risks related to underlying diseases, ICU-specific treatment modalities, and mortality remains to be investigated in dialysis-requiring AKI patients within ICU setting [9]. Shorter LOS in ICU and hospital observed in CRRT group could also be attributed to more severe state of illness and earlier death. Regarding these complex interactions and inherent limitations for trial design, selection of patient subgroups most likely to benefit from different HD methods and sequential or hybrid use of RRT modalities have been proposed as investigational areas instead of head-to-head comparisons of different RRT modalities [31-33].

While creatinine levels at HD initiation were almost three times of the baseline values in all patients, significantly lower levels of creatinine and BUN was detected at HD initiation in the CRRT group. This finding could be explained by the different nutritional or metabolic state of RRT groups and the dilutional effect of volume overload to correct severe hypotension or hypovolemia in the CRRT patients [34]. Unfortunately, further interpretation is not possible as reliable data for fluid admission and nutritional interventions were not available in our patient records.

Limitations

Limitations of this study include absence of data for urine output, fluid administration, and nutritional management, lack of long-term follow-up for survival and development of kidney failure, and finally a possible patient selection bias as this study was conducted in a single tertiary institution.

Conclusion

We found that patients admitted to the ICU with D-AKI suffered from considerable risk factors with poor prognosis and preference of CRRT, as RRT could be an indicator for increased in-hospital mortality. Prospective studies with large groups to investigate dialysis-requiring high-risk AKI in critical illness are required. Prevention of infectious complications and sepsis may lower the burden of morbidity and incidence of D-AKI and hereby improve outcome in AKI patients admitted to the ICU.

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