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Original Article

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Clinical Features and Outcomes in Acute Kidney Injury Patients Who Underwent Urgent Dialysis in a Regular Hemodialysis Unit

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Abstract

Objective: An urgent hemodialysis (uHD) procedure is performed in acute kidney injury (AKI) with life-threatening complications. In this study, we aimed to investigate the clinical and laboratory findings that were associated with mortality in a regular HD unit.

Materials and Methods: In total, 811 patients who underwent uHD were included in the study. The indications for uHD, demographic data, comorbidities, and pre- and post uHD laboratory results were obtained from patients' registry files. Clinical outcomes regarding the renal status after uHD, patient survival, and causes of mortality were evaluated.

Results: The most common uHD indication was hypervolemia; 276 patients died in the follow-up period, and the most common cause of death was progression of underlying disorders. The most frequent renal outcome was dialysis dependency. Oliguria and hypotension during uHD were associated with an increased likelihood of mortality based on an age-adjusted analysis. According to a multivariate analysis, malignancy, presence of crackle, and prerenal AKI were independently associated with increased mortality.

Conclusion: Due to high mortality in AKI, a prompt diagnosis and appropriate management of the patients are of paramount importance. Anticipation of the clinical risk factors associated with increased mortality may help in better stratification of patients at high risk.

Keywords: Acute kidney injury, comorbidity, hemodialysis, mortality, outcome

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INTRODUCTION

Acute kidney injury (AKI) is a usually reversible decline in the glomerular filtration rate (GFR). An impaired excretion of metabolic waste products results in an elevation of serum blood urea nitrogen and creatinine. A decline in the GFR also results in the dysregulation of extracellular volume and electrolytes. Supportive management is provided for patients with AKI. Renal replacement therapy (RRT) is indicated in patients with severe kidney injury. An urgent hemodialysis (uHD) treatment is defined as a dialysis session performed either in acute AKI or in acute or chronic renal failure (ARF or CRF) with life-threatening complications, such as severe hyperkalemia, severe metabolic acidosis, refractory pulmonary edema, uremic symptoms and signs (e.g., pericarditis, bleeding, encephalopathy, or an otherwise unexplained decline in the mental status), overdose with a dialyzable drug/toxin, or malign hypercalcemia. The initiation of RRT in patients with AKI prevents uremia and immediate mortality from the adverse complications of renal failure.

Multiple modalities of RRT, such as intermittent HD (IHD), continuous renal replacement therapies (CRRTs), and hybrid therapies, are available. In recent years, IHD and various types of hemodiafiltration have been used

for urgent dialysis. Slow-continuous hemodiafiltration and some HD techniques have been particularly used for intensive care unit patients who are in a hypercatabolic stage and unstable. Survival in patients with AKI has improved with advances in these dialysis techniques. Nevertheless, mortality in patients with AKI remains high, exceeding 40%-50%, particularly in severely ill patients. The underlying disorders, such as diabetes mellitus; hypertension; vasculitis; and comorbidities, including congestive heart failure, ischemic heart disease, sepsis, malignancy, chronic liver disease, and cerebrovascular disease, also contribute to the mortality in patients with AKI. There are several studies examining the mortality in AKI in the intensive care setting (1-4).

However, data on the mortality of the patients undergoing treatment in the regular HD units are scarce.

In this retrospective study, we aimed to investigate the demographic characteristics, clinical manifestations, laboratory findings, and outcomes of patients with AKI who underwent uHD, specifically intermittent uHD.

MATERIALS AND METHODS

The features of study hospital recruited during the study period (sickbeds, hospitalization, birth and death rates, and number of operations and admissions to the outpatient clinics) were obtained from statistical data of the hospital.

Adult patients (aged>18 years) who were referred from the emergency department and underwent intermittent uHD in our regular HD unit between January 2005 and December 2015 were retrospectively evaluated by examining the medical records. Data from the medical records were collected using standardized forms by a physician blinded to the outcome of the patients.

The indications for uHD were refractory hyperkalemia (plasma potassium concentration>6.5 mEq/L or rapidly rising potassium levels); refractory metabolic acidosis (pH<7.1); refractory volume overload; uremic symptoms and signs, such as encephalopathy, nausea, vomiting, and pericarditis; and refractory hypercalcemia. Patients on chronic maintenance HD were excluded from the study. In addition, critically ill patients at first admission (presence of hemodynamic instability and/or sepsis and/or multiorgan dysfunction syndrome) who needed CRRTs were excluded from the study. Patients who underwent uHD because of intoxication were also excluded from the study.

The demographic findings (age, gender, and type of residency as urban or rural) and clinical findings during the hospital course, such as mental status, peripheral edema, skin turgor, icterus, cyanosis, jugular venous distention, radial pulse, mean arterial pressure (MAP), body temperature, respiratory rate, pleural effusion, crackle, third heart sound, pericardial rubbing, ascites, hepatomegaly, and urinary output were obtained from the hospital medical records.

MAP was calculated using the following equation:

MAP=DP+1/3 (SP-DP)

(DP, diastolic pressure, mmHg; SP, systolic pressure, mmHg)

Hypotension was defined as MAP <70 mmHg (5) and hypertension as MAP >107 mmHg (6). A tympanic membrane temperature of >37.7°C was defined as hyperthermia and <35.0°C as hypothermia. Tachypnea was defined as a respiratory rate >20 breaths per minute. Oliguria was defined as a urine output below 400 mL/day.

The personal history of comorbidities (chronic kidney disease, diabetes mellitus, systemic hypertension, malignancy, connective tissue disease, chronic liver disease, coronary heart disease, congestive heart failure, chronic obstructive lung disease, and cerebrovascular disease) was recorded.

Laboratory findings of serum urea; creatinine; uric acid; glucose; sodium; potassium; calcium; phosphorus; aspartate transaminase (AST); alanine transaminase (ALT); albumin; C-reactive protein (CRP); creatine phosphokinase; hemoglobin; white blood cell; platelet counts; international normalized ratio; activated partial thromboplastin time; arterial values of pH and bicarbonate; and serological markers for hepatitis B, hepatitis C, and human immunodeficiency viruses at the time of diagnosis were recorded.

Laboratory findings, such as proteinuria and microscopic hematuria, were also recorded. Proteinuria was detected using dipstick urinalysis. Microscopic hematuria was accepted as the excretion of more than two red blood cells per high-power field in a centrifuged urine specimen.

The same physician who had experience in the care of acute HD re-evaluated all the files according to The Kidney Disease: Improving Global Outcomes guideline.

AKI was evaluated with the criterion defined below:
1. In patients with prehospital data, the mean outpatient serum creatinine value of 7-365 days before hospitalization was used in choosing a prehospital reference creatinine (7) and an increase in the serum creatinine level by ≥1.5 times the baseline level, which is presumed to have occurred within the prior 7 days was used for defining AKI (8).

2. In patients without prehospital data, urine volume of <0.5 mL/kg/h for 6 hours was considered for the diagnosis of AKI (8). An increase in the serum creatinine value was also evaluated during that period.

The type of AKI (prerenal, intrinsic and postrenal) was investigated. Prerenal disease was defined as the accumulation of nitrogenous waste products in any state of any process that

decreased blood delivery to the kidneys. Intrinsic renal disease was defined as sudden loss in the kidney function due to the direct damage to the kidneys. Postrenal disease was defined as loss in kidney function due to an obstruction in the urinary tract.

HD prescription (frequency and duration of HD, ultrafiltration rates, blood and dialysate flow rates, type and surface area of membranes, and type of anticoagulation); vascular access (femoral or internal jugular vein catheters); and HD complications, such as hypotension (Kidney Disease Outcomes Quality Initiative (K/DOQI) define the presence of a decrease in the systolic blood pressure ≥20 mmHg or a decrease in the MAP by 10 mmHg, which is associated with clinical events and the need for nursing interventions), muscle cramps, nausea and vomiting, chest pain, arrhythmias, convulsion, and hypoglicemia, were obtained from medical records.

The clinical outcome and the renal status (complete recovery, partial recovery, and dialysis dependency), patient survival (death or alive), and causes of mortality were recorded. Complete recovery was defined as the normalization of renal function. Partial recovery was defined as the persistence of high urea and creatinine levels but not requiring dialysis. Dialysis dependency was defined as the requirement of dialysis to maintain life. Moreover, the clinical outcome (death or survival) and causes of mortality were investigated.

Statistical Analysis

The clinical and laboratory findings were compared between the patients who survived and who did not survive for determining the factors associated with mortality. Clinical and laboratory characteristics were compared using the Student's t-test or Mann-Whitney U test according to the distribution of data. Differences in categorical variables were evaluated using the Chi-square analysis and Fisher's exact test. Age-adjusted odds ratio (OR) for mortality was obtained using regression logistic models. Variables that were significantly associated with mortality ($p<0.05$) in age-adjusted analysis were used to construct multivariate models. Multivariate logistic regression was used to evaluate the determinants of mortality. Forward selection was used in multivariate models. The relation between numerical variables and clinical outcome was evaluated using the Pearson correlation test. The relation between nominal variables and clinical outcome was analyzed using the Spearman's rho correlation test.

Data were expressed as mean±standard deviation. A $p<0.05$ was accepted as significant. All computations were conducted using the Statistical Package for Social Sciences (SPSS®) software for Windows®, version 16.0 (SPSS Inc., Chicago, IL, USA).

This study was approved by the local ethics committee (approval no: 16798/2009).

RESULTS

The total number of sickbeds were 1 358 in the study hospital. During the 10-year study period of January 2005-December 2015, there were 6 105 152 admissions to the outpatient clinics, 433 692 patients were hospitalized, 12 846 births were recorded, and 270 916 operations were performed. Furthermore, 9219 patients who were hospitalized died, and the rate of mortality (death) was 2.1%.

A total of 820 patients who underwent uHD during the same period were evaluated. The uHD procedure was performed in 811 patients for AKI and in 9 patients for intoxication (3 lithium, 1 salicylate, 1 barbexaclon, and 4 mushroom cases). Nine patients with intoxication were excluded from the study. A total of 811 patients with AKI (309 females and 502 males) were included in this study. The demographic, clinical, and laboratory findings of 811 patients who underwent uHD are shown in Table 1. The pre-existing comorbid conditions were as follows: hypertension in 300 (36.9%) patients, malignancy in 199 (24.5%), diabetes mellitus in 213 (26.2%), coronary heart disease in 52 (6%), congestive heart failure in 44 (5.5%), chronic liver disease in 36 (4.5%), chronic obstructive pulmonary disease in 18 (2%), cerebrovascular disease in 13 (1.5%), and connective tissue diseases in 13 (1.5%).

The types of cancers were as follows: genitourinary cancer in 84 patients (32.5%), multiple myeloma in 50 (19.5%), gastrointestinal cancer in 46 (18%), leukemia/lymphoma in 25 (10%), lung cancer in 18 (7%), breast cancer in 13 (5%), and other cancers in 21 (8%).

The most common symptoms during the hospitalization period were as follows: nausea and vomiting in 494 (80%) patients, anorexia in 354 (48%), dyspnea in 320 (43%), fatigue in 319 (43%), palpitation in 149 (20%), and pruritus in 118 (16%).

Upon the initial physical examination, peripheral edema was present in 405 (50%) patients, crackle in 275 (33%), hypertension in 250 (31%), tachypnea in 235 (28%), tachycardia in 130 (16%), increased jugular venous distention in 67 (8%), ascites in 41 (5%), hyperthermia in 40 (5%), unconsciousness in 41 (5%), hypotension in 26 (3%), decreased skin turgor in 25 (3%), icterus in 24 (3%), third heart sound in 16 (2%), and pericardial rubbing in 8 (1%).

The uHD indications were as follows: hypervolemia in 250 (30.8%) patients, uremic symptoms in 236 (29%), refractory hyperkalemia in 192 (23%), refractory metabolic acidosis in 105 (14.6%), refractory hypercalcemia in 13 (1.6%), and pericarditis in 11 (1%).

The types of AKI were as follows: prerenal in 131 (16%) patients, intrinsic in 415 (51%), and postrenal in 228 (28%). Further, the etiology of AKI in 31 (5%) patients was unknown. The underlying causes of the need for uHD are shown on Table 2.

Table 1. Demographic, clinical, and laboratory findings of 811 patients who underwent urgent hemodialysis

Findings	
Age (years) (mean±SD)	57.6±16.8
Gender (female/male) n (%)	309 (38)/502 (62)
Type of residency (urban/rural) n (%)	695 (85.7)/116 (14.3)
Mean arterial pressure (mmHg) (mean±SD)	101.3±15.9
Oliguria/nonoliguria n (%)	255 (31.5)/556 (68.5)
Proteinuria/hematuria[a] n (%)	190 (34.1)/150 (26.9)
Urea (mg/dL) (mean±SD)	220.4±63.5
Creatinine (mg/dL) (mean±SD)	7.6±2.3
Uric acid (mg/dL) (mean±SD)	7.2±2.1
Glucose (mg/dL) (mean±SD)	112.2±52.4
Sodium (mEq/L) (mean±SD)	134.5±4.5
Potassium (mEq/L) (mean±SD/median, min–max)	7±0.5[b]/5, 2.7-9.3
Calcium (mg/dL) (Mean±SD/median, min–max)	17.8±1.5[c]/8.2, 4.9-22
Phosphorus (mg/dL) (mean±SD)	5.2±1.3
ALT (IU/L) (median, min–max)	15, 5-1630
AST (IU/L) (median, min–max)	18, 3-1273
Albumin (g/dL) (mean±SD)	2.5±0.8
CRP (mg/L) (mean±SD)	79.4±71.2
CPK (U/L) (median, min–max)	57, 6-12.800
Arterial blood pH (mean±SD)	7.24±0.33
Arterial blood HCO_3 (mEq/L) (mean±SD)	14.7±4.6
Hemoglobin (g/dL) (mean±SD)	9.1±1.4
Leukocyte (mm^3) (mean±SD)	10100±5000
Thrombocyte ($\times 10^3/\mu L$) (mean±SD)	231000±120500
INR (mean±SD)	1.11±0.21
aPTT (s) (mean±SD)	39.6±8.2
HBsAg-positive n (%)	25 (3)
Anti-HCV positive n (%)	12 (1.4)
HIV positive n (%)	0

[a]Hematuria and proteinuria were evaluated in nonoliguric 556 patients
[b]mean potassium values of patients who underwent urgent hemodialysis due to hyperkalemia
[c]mean calcium values of patients who underwent urgent hemodialysis due to hypercalcemia
CRP: C-reactive protein; CPK: creatine phosphokinase; INR: international normalized ratio; aPTT: activated partial thromboplastin time; SD: standard deviation; ALT: alanine transaminase; AST: aspartate transaminase; HBsAg: hepatitis B antigen; HCV: hepatitis C virus; HIV: human immunodeficiency virus

Table 2. Underlying causes of the need for urgent hemodialysis

Etiologies of acute kidney injury	n=811
Prerenal etiologies	131 (16)
Dehydration	44
Bleeding	39
Heart failure	14
Impairment of autoregulation with drugs	12
Hepatorenal syndrome	22
Renal etiologies	415 (51)
Systemic vasculitis	13
Glomerulonephritis	9
Acute interstitial nephritis	21
Acute tubular necrosis (ischemic/toxic)	100
Rhabdomyolysis	27
Thrombotic thrombocytopenic purpura	12
Renal vein thrombosis	5
Sepsis	156
Cholesterol embolism	4
Multiple myeloma	30
Radiocontrast induced nephropathy	18
Hemoglobinuria	6
Tumor lysis syndrome	14
Postrenal etiologies	228 (28)
Stones	39
Urological tumors (benign or malignant)	74
Nonurological malignant tumors	110
retroperitoneal fibrosis	5
Unknown etiology	31 (5)

Right internal jugular catheterization (n: 567 [70%]) was the prominent vascular access route. The subclavian and femoral veins were used in the rest of the patients (n: 178 [22%], n: 66 [8%], respectively). Regarding the features of uHD sessions, the number of total sessions was 7.18±7.16, with 17.51±12.3 hour duration. Two- to five-hour uHD sessions were performed. Blood flow rates were maintained between 200 mL and 350 mL/min with various ultrafiltration rates (0-4 000 mL), which were calculated according to the clinical and physical signs of the patients. The uHD procedure was performed at the dialysate flow rate of 500 mL/min. Synthetic low-flux biocompatible membranes were used during each of the uHD sessions. The membranes had effective surface areas of 1.4-2.1 m^2 and values

of the dialyzer mass transfer-area coefficient K_0A ranging from about 850 to 1265. Patients underwent dialysis using a bicarbonate-based dialysate and 0-4 000 units of standard heparin per session based on the clinical findings.

HD complications were as follows: hypotension in 119 (14.5%) patients, nausea and vomiting in 41 (5%), hypoglycemia in 36 (4.5%), fever and chills in 28 (3.5%), chest pain in 25 (3%), convulsion in 20 (2%), muscle cramps in 19 (2%), headache in 19 (2%), arrhythmias in 14 (1.5%), and others in 14 (1.5%).

Patients with AKI were hospitalized for at least 2 weeks. Overall, 1.0-1.5 g/kg/day protein intake with a goal of total energy intake of 25-30 kcal/kg/day was planned for patients during hospitalization.

Among 811 patients who underwent uHD, 276 (34%) patients died. The most common causes of deaths were as follows: progression of underlying disorders in 132 (48%) patients, infections in 79 (28%), cardiovascular diseases in 32 (12%), metabolic disorders in 28 (10%), cerebrovascular diseases in 3 (1%), and other causes in 2 (1%).

The renal outcomes of 535 patients who survived were as follows: complete recovery in 63 (12%) patients, partial recovery in 105 (23%), and dialysis dependency in 349 (65%). The mean recovery time was 12 days for ARF

The demographic characteristics, physical examination, and laboratory findings of patients; etiologies of AKI; indications of uHD among patients who survived and died; and comorbid diseases and their mortality rates are shown in Tables 3-8.

Among the 535 patients who survived, 400 were nonoliguric 135 were oliguric. In contrast, among the 276 patients who died, 120 patients were oliguric and the remaining were nonoliguric. Oliguria was associated with an increased likelihood of mortality (p=0.000, r=0.172, OR: 2.157, 95% confidence interval [CI]: 1.557-2.990).

Among the 535 patients who survived, 58 patients experienced hypotension during the uHD. However, among the 276 patients who died, 60 patients experienced hypotension during the uHD. Hypotension during the uHD was associated with an increased likelihood of mortality (p=0.002, r=0.114, OR: 1.955, 95% CI: 1.274-3.001).

There is a strong association between age and mortality. Therefore, we analyzed the study parameters following age adjustment.

Age-adjusted ORs for mortality of the different study parameters are shown in Tables 3-7. Malignancy was associated with mortality following age adjustment analysis. However, the presence of systemic hypertension and diabetes mellitus, which showed borderline significance, was associated with decreased mortality among comorbid diseases (Table 3).

Patients who died were more likely to have demonstrated unconsciousness, peripheral edema, icterus, tachycardia, hypo-

Table 3. Demographic characteristics and comorbid diseases of patients who survived and those who died

Characteristics	Patients who survived (n=535)	Patients who died (n=276)	p[a]	Adjusted for age p[b] OR (95% CI)
Age (years)	54.0±17.3	61.3±12.6	0.000	1.029 (1.019-1.040)
Gender (male/female)	337 (62.9%)/198 (37.1%)	174 (63.1 %)/102 (36.9%)	NS	0.973 (0.704-1.345)
Type of residency (urban/rural)	447 (83.5%)/88 (16.5%)	239 (86.6%)/37 (13.4%)	NS	0.903 (0.576-1.417)
Diabetes mellitus	149 (27.8%)	64 (23.1%)	NS	0.682 (0.466-0.997)
Systemic hypertension	225 (42%)	75 (27.1%)	0.003	0.506 (0.356-0.720)
Malignancy	104 (19.4%)	95 (34.4%)	0.000	2.172 (1.532-3.081)
Connective tissue diseases	11 (1.6%)	2(0.7%)	0.048	0.000
Chronic liver diseases	24 (4.4%)	12 (4.3%)	NS	1.046 (0.475-2302)
Coronary heart disease	34 (6.3%)	18 (6.5%)	NS	0.862 (0.451-1.646)
Congestive heart failure	26 (4.8%)	18 (6.5%)	NS	1.330 (0.681–2.597)
COPD	10 (1.8%)	8 (2.8%)	NS	1.523 (0.535-4.337)
Cerebrovascular disease	9 (1.6%)	4 (1.6%)	NS	1.038 (0.293-3.673)

NS: nonsignificant; COPD: chronic obstructive pulmonary disease; CI: confidence interval; OR: odds ratio
[a]chi-square test,
[b]age-adjusted logistic regression test

Table 4. Physical examination findings of patients who survived and those who died

Findings	Patients who survived (n=535)	Patients who died (n=276)	p[a]	Adjusted for age	
				OR (95% CI)	p[b]
Unconsciousness	14 (2.6%)	27 (9.7%)	0.000	3.519 (1.72-7.186)	0.001
Peripheral edema	247 (46.1%)	158 (57.2%)	0.001	1.522 (1.109-2.089)	0.009
Decreased skin turgor	15 (2.8%)	10 (3.6%)	NS	1.050 (0.435-2.538)	NS
Icterus	8 (1.4%)	16 (5.7%)	0.004	3.340 (1.294–8.618)	0.013
Increased jugular venous distention	47 (8.7%)	20 (7.2%)	NS	0.695 (0.381-1.267)	NS
Tachycardia	65 (12.1%)	65 (23.5%)	0.001	2.513 (1.667-3.790)	0.000
MAP (mmHg)	101.2±12.7	94.3±18.1	0.000	0.975 (0.966-0.985)	0.000
Hypotension	6 (1.2%)	20 (8%)	0.000	6.9 (2.7-17.9)	0.000
Hypertension	184 (34.3%)	66 (23.9%)	0.004	0.67 (0.471-0.955)	0.027
Body temperature (hyperthermia)	20 (3.7%)	20 (7.2%)	NS	2.369 (1.2-4.677)	0.013
Respiratory rate (tachypnea)	124 (23.1%)	111 (40.2%)	0.000	2.256 (1.605-3.172)	0.000
Pleural effusion	37 (6.9%)	30 (10.8%)	NS	1.601 (0.950-2.696)	NS
Crackle	155 (28.9%)	120 (43.4%)	0.000	1.690 (1.21-2.34)	0.002
Third heart sound	8 (1.4%)	8 (2.8%)	NS	2.301 (0.847-6.249)	NS
Pericardial rubbing	4 (0.8%)	4 (1.4%)	NS	1.508 (0.314-7.247)	NS
Ascites	20 (3.7%)	21 (7.6%)	0.010	2.229 (1.158-4.289)	0.016
Hepatomegaly	16 (2.9%)	7 (2.5%)	NS	0.754 (0.302-1.886)	NS

MAP: mean arterial pressure; NS: nonsignificant; CI: confidence interval; OR: odds ratio
[a]chi-square test,
[b]age-adjusted logistic regression test

tension, hyperthermia, tachypnea, crackle, and ascites during the hospitalization.

We demonstrated that the patients who survived were more likely to have demonstrated hypertension and higher MAP (Table 4).

While higher ALT, AST, and leukocyte values were associated with increased mortality among laboratory findings, higher hemoglobin and creatinine values were associated with decreased mortality (Table 5).

In terms of etiologies of AKI, while prerenal AKI was associated with increased mortality, postrenal AKI was associated with decreased mortality (Table 6). Regarding the analysis of subgroups among etiologies of ARF using the Pearson and Spearman correlation tests, sepsis (p=0.000, r0.363), acute tubular necrosis (ATN, p=0.000, r=0.154), heart failure (p=0.015, r=0.09), bleeding (p=0.000, r=0.178), and rhabdomyolysis (p=0.024, r=0.178) were associated with increased mortality. In contrast, multiple myeloma (p=0.016, r=−0.89) and kidney stone (p=0.000, r=−0.138) were associated with decreased mortality.

While hyperkalemia and hypervolemia were associated with mortality, the presence of uremic symptoms was associated with decreased mortality regarding indications of uHD (Table 7).

Oliguria was associated with an increased likelihood of mortality based on the age-adjusted analysis (p=0.000, OR: 2.111; 95% CI: 1.513-2.945).

Hypotension during uHD was associated with an increased likelihood of mortality with age-adjusted analysis (p=0.002, OR: 1.973; 95% CI: 1.271-3.061).

Finally, we performed multivariate logistic regression. According to the multivariate analysis, malignancy (OR: 8.731; 95% CI: 1.384 to 55.074; p=0.021), presence of crackle (OR: 14.998; 95% CI: 1.916-117.433; p=0.010), and prerenal AKI (OR: 50.188; 95% CI: 7.216-349.047; p=0.000) were independently associated with increased mortality.

DISCUSSION

The etiologies of the emergent dialysis and AKI showed differences according to the geographical features and socioeconom-

Table 5. Laboratory findings of patients who survived and those who died

Findings	Patients who survived (n=535)	Patients who died (n=276)	p[a]	Adjusted for age	
				OR (95% CI)	p[b]
Urea (mg/dL)	221.9±61.0	224.3±2	0.400	1.001(0.998-1.003)	0.509
Creatinine (mg/dL)	8.4±3.3	7.2±3.3	0.005	0.950(0.904-1.000)	0.049
Uric acid (mg/dL)	7.2±2.1	8.1±2.3	0.090	1.199 (0.975-1.474)	0.086
Glucose (mg/dL)	111.3±46.4	125.4±67.4	0.112	1.005 (0.998-1.011)	0.142
Sodium (mEq/L)	133.0±4.4	131.4±6.2	0.140	0.979 (0.952-1.007)	0.142
Potassium (mEq/L)	4.8±1.1	4.9±1.2	0.100	1.102 (0.971-1.250)	0.134
Calcium (mg/dL)	7.9±1.4	8.1±1.2	0.435	1.070 (0.89-1.286)	0.471
Phosphorus (mg/dL)	5.5±1.7	5.2±2.2	0.455	0.937 (0.718-1.223)	0.634
ALT (IU/L) (median, min–max)	14, 5–116	18, 5–1630	0.008	1.021 (1.001-1.032)	0.000
AST (IU/L) (median, min–max)	16, 3–182	27, 5–1273	0.000	1.023 (1.010-1.035)	0.000
Albumin (g/dL)	2.6±0.3	2.6±0.3	0.690	0.969 (0.727-1.291)	0.830
CRP (mg/L)	67±78.1	96.8±70.5	0.03	1.005 (1.000-1.010)	0.053
CPK (/L (median, min–max)	53, 6–12800	3130, 2000–4260	0.450	1.000 (1.000-1.001)	0.394
Arterial pH	7.21±0.32	7.26±0.11	0.345	7.840 (0.180-342.139)	0.285
Arterial HCO_3 (Eq/L)	14.1±4.1	15±4.1	0.250	1.036 (0.960-1.118)	0.363
Hemoglobin (g/dL)	9±1.2	8.8±1.5	0.165	0.871 (0.759-0.999)	0.048
Leukocyte (/mm^3)	9740±4990	12350±4643	0.006	1.000 (1.000-1.000)	0.007
Thrombocyte (×10^3/µL)	226000±114160	201000±135680	0.150	1.000 (1.000-1.000)	0.167
INR	1.15±0.24	1.10±0.20	0.675	0.290 (0.002–54.418)	0.643
aPTT (sec)	40±8.2	42.2±9	0.594	1.031 (0.917-1.159)	0.612

NS: nonsignificant; CI: confidence interval; OR: odds ratio; CRP: C-reactive protein; CPK: creatine phosphokinase; INR: international normalized ratio; aPTT: activated partial thromboplastin time; ALT: alanine transaminase; AST: aspartate transaminase
[a]chi-square test,
[b]age-adjusted logistic regression test

ic status. In our study, intrinsic factors were the most common causes of AKI. A study by Liano et al. in Spain showed that the etiologies of AKI were ATN (45%), prerenal AKI (21%), and obstructive AKI (10%) (9). Another study by Jayakumar et al. (10) in South India revealed that acute diarrhea was the most common reason for AKI among 1112 patients who were being followed in 1995-2004; drugs, glomerulonephritis, sepsis, snakebites, leptospirosis, and malaria were other etiologies for ARF. In contrast, sepsis, volume depletion, obstructive uropathy, heart failure, acute glomerulonephritis, and severe malaria were the most common causes of AKI in a retrospective study by Osman et al. (11) in Sudan.

Our study revealed that more number of men underwent uHD than did women. In different studies, the ratios of men undergoing uHD were between 54% and 76% (10-15).

The age range of patients who underwent uHD was from 40 years to 74 years. The mean age was between 37.08 and 68.5 years in various studies (13, 14, 16). Obviously, this is related to the clinical setting of the study.

In our study, the indications for uHD were hypervolemia, uremic symptoms, hyperkalemia, and metabolic acidosis. In line with our findings, fluid overload was a major indication for RRT initiation in the other studies (17-20).

The most common comorbid conditions in patients with renal failure on uHD were hypertension, malignancy, and diabetes mellitus. The same comorbid conditions were demonstrated in another study by Cruz DN et al. (13).

Oliguria was detected in 31.5% of the patients who underwent uHD. In other studies, the oliguria ratio was between 19.7% and 60% (13, 21).

Table 6. Etiologies of AKI in patients who survived and those who died

Etiologies	Patients who survived (n=535)	Patients who died (n=276)	p[a]	Adjusted for age	
				OR (95% CI)	p[b]
Prerenal	66	65	0.000	2.254 (1.492-3.406)	0.000
Intrinsic	270	145	NS	1.114 (0.815-1.524)	NS
Postrenal	176	52	0.000	0.194 (0.119-0.315)	0.000
Unknown	21	10	NS	0.779 (0.354-1.712)	NS

NS: nonsignificant; AKI: acute kidney injury; CI: confidence interval; OR: odds ratio
[a]chi-square test
[b]age-adjusted logistic regression test

Table 7. Indications of urgent hemodialysis of patients who survived and those who died

Indications	Patients who survived (n=535)	Patients who died (n=276)	p[a]	Adjusted for age	
				OR (95% CI)	p[b]
Hyperkalemia	113 (21.1%)	79 (28.6%)	0.009	1.582 (1.108-2.259)	0.012
Metabolic acidosis	91 (17%)	29 (10.5%)	0.032	0.653 (0.394-1.085)	NS
Hypervolemia	145 (27%)	105 (38%)	0.005	1.461 (1.046-2.039)	0.026
Uremic symptoms	184 (34%)	52 (18.8%)	0.000	0.476 (0.327-0.693)	0.000
Hypercalcemia	9 (1.6%)	4 (1.4%)	NS	0.575 (0.058-5.650)	NS
Uremic pericarditis	6 (1.1%)	5 (1.8%)	NS	1.508 (0.314-7.247)	NS

CI: confidence interval; OR: odds ratio
[a]chi-square test,
[b]age-adjusted logistic regression test

Table 8. Comorbid diseases and mortality rates of patients

Comorbid disease	Patients who survived (n)	Patients who died (n)	Mortality rates (%)
Diabetes mellitus	149	64	30%
Systemic hypertension	225	75	25%
Malignancy	104	95	47.7%
Chronic liver disease	24	12	33.3%
Coronary heart disease	34	18	34.6%
Congestive heart failure	26	18	41%
COPD	10	8	44.4%
Cerebrovascular disease	9	4	30.7%

COPD: chronic obstructive pulmonary disease

In our cohort, the mortality rate was 34%. The common causes of death were progression of underlying diseases, infections, and cardiovascular diseases. The ratio of death was 45% and 44%-56% in the studies by Liano et al. (9) and Chow et al., (22) respectively.

The renal outcomes of the patients were as follows: 12% of the patients recovered completely, 88% had CRF (67% of them were dialysis-dependent, 21% of them were dialysis-independent). In a prospective study by Nash et al., with regard to hospital-acquired renal insufficiency, 38.6% of 332 patients completely recovered, 22.6% showed partial recovery, 16.7% were discharged with elevated creatinine values, and 2.7% of them had CRF (12). These findings were contrasting to those of our study. Since our study was performed in a tertiary referral hospital, more severe, complicated cases with multiple comorbid diseases, were admitted to the emergency services. Therefore, the lower renal recovery rate can be explained by the high prevalence of underlying kidney disease among AKI etiologies. Moreover, in the study by Nash et al., the most common causes of AKI were reversible etiologies, such as decreased renal perfusion, medications, surgery, and radiographic contrast media.

Advanced age was shown to increase mortality in our study, which was similar to the previous studies (23-25). However, since there is a strong association between age and mortality, we analyzed the study parameters following age adjustment.

According to the age-adjusted analysis in our study, co-existing malignancy increased mortality and was also associated with mortality in the study of Ng KP et al. (14) and Wang et al. (26).

Mortality was higher in hypotensive patients. Hypotension was also associated with mortality in the studies by Liano (9) and Wang (26).

We demonstrated that the patients who survived were more likely to have hypertension or higher MAP values during the initial physical examination. A logical explanation of this result may be that these hypotensive patients had severe infection (sepsis) and they were susceptible to multiorgan failure. In addition, the presence of diabetes mellitus was slightly associated with reduced mortality rates. Frequent follow-ups of these patients with a multidisciplinary approach (endocrinological, nephrological, cardiac, neurological, and ophthalmologic) may explain this paradoxical phenomenon.

A low creatinine value was also associated with increased mortality in our study. Cruz et al. (13) also found an association between low creatinine levels and increased mortality in their study. Other authors have also stated a similar pattern in their studies (27-29). They hypothesized that low serum creatinine, particularly after adjustment for age and gender, reflects loss of muscle mass and a hypercatabolic status of these patients contributing to increased mortality. However, it could also be related to volume overload and its diluting effect on the serum creatinine.

Infections was one of the leading causes of death in our study. Therefore, the presence of hyperthermia; tachycardia; tachypnea; and high ALT, AST, and leukocyte values, which may reflect severe infection and multiorgan failure, was associated with increased mortality. However, elevated CRP was not associated with increased mortality in our study. The serum CRP value was also not associated with mortality in the study by Wang et al. (26).

We showed that patients with AKI due to prerenal etiologies have increased mortality. The presence of concomitant severe infection or dehydration due to severe vomiting and diarrhea in malignancy or congestive heart failure or hepatorenal syndrome in which inappropriate accumulation of blood in the third space is the main problem, may explain this situation. However, patients with postrenal etiologies have decreased mortality. A more rapid management and easier treatment of postrenal causes than other causes may explain this result.

We demonstrated that the presence of hyperkalemia and crackles possibly related to hypervolemia, which may be a surrogate for severe oliguric kidney failure, was associated with mortality.

The presence of oliguria was associated with increased mortality in our study. Two previous studies also showed an association between oliguria and increased mortality (21, 26).

In our cohort, hypotension during uHD was associated with increased mortality. The presence of hemodynamically unstable patients with malignancy and/or sepsis during dialysis may explain this situation. According to previous studies, on maintenance dialysis treatment, increased morbidity and mortality of patients are associated with intradialytic hypotension episodes (30, 31).

According to the multivariate analysis, malignancy, presence of crackles, and prerenal AKI were independently associated with increased mortality. Prerenal AKI related to congestive heart failure with crackles or reduced renal perfusion due to systemic vasodilation that is seen during the course of sepsis may explain the association. Malignancy is associated with AKI via different pathways. Malignancy may lead to water loss through vomiting or diarrhea related to chemotherapeutic agents. Malignancy, which compromises immunity, may be concomitant with sepsis that cause systemic hypotension, probably causing reduced renal perfusion. In contrast, hypercalcemia as a result of parathyroid hormone release, which increases bone resorption and renal tubular resorption of calcium, is seen in 10%-30% of malignancies. This can lead to a prerenal state of AKI due to vasoconstriction as well as volume depletion from natriuresis and diuresis (32, 33).

The most important limitation of our study is the retrospective nature. It may not be appropriate to infer about the causality in the retrospective studies.

CONCLUSION

The mortality rate is high in AKI. A prompt diagnosis and appropriate management of these patients are of paramount importance. The anticipation of the clinical risk factors that are associated with increased mortality may be helpful in better stratification of patients at high risk.

Ethics Committee Approval: Ethics Committee approval was received for this study from the Ethics Committee of İstanbul University-Cerrahpaşa, Cerrahpaşa School of Medicine (approval no: 16798/2009).

Informed Consent: Informed consent was obtained from all the patients included in the study.

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