Emergency Medicine Investigations

Research Article

Acute Kidney Injury and Associated Factors Depending on Mechanical Ventilation in Intensive Care Units, 3-year-long Retrospective Analysis

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Abstract

Objective: Acute Kidney Injury (AKI) is one of the subjects that nephrology works on often because of creating severe systemic and renal damage. We aimed to investigate the risk of developing AKI and related factors depending on mechanical ventilation in the intensive care unit.

Design: Retrospective study.

Subject: 300 patient's files were examined.

Intervention: Between January 1, 2015, and June 31, 2017, 300 cases were divided into two groups. 100 cases were control group (non-MV group), 200 cases were case group (MV group).

Main Outcome Measures: Demographic data, BUN/Creatinine ratio, APACHE II score, number of MV days, total hospitalization days, need hemodialysis or not, accompanied comorbid factors were recorded.

Results: As the number of days of MV and APACHE II score increases, the need for hemodialysis increases (p < 0.001, p < 0.001). At the same time, as the average age is increasing also needs for hemodialysis increase (p = 0.003). Also, the need for hemodialysis increases as the duration of hospitalization increases (p = 0.002µ) the risk of receiving hemodialysis is 129.76 times higher in mechanical ventilation connection compared to no connection, 2.80 times higher in patients with diabetes compared to nondiabetics, 19.69 times higher in sepsis compared to patients without sepsis, 9.73 times higher in patients with BUN/Creatinine ratio (BCR) above 10 compared to under 10

Conclusion: To reduce the incidence of AKI depending on mechanical ventilation, non-invasive mechanical ventilation, advanced monitorization facilities should be present for each intensive care unit.

Keywords: Acute Renal Failure; Breath Insufficiency; Renal Replacement Therapy

Abbreviations:

COPD	:	Chronic Obstructive Pulmonary Disease
DM	:	Diabetes Mellitus
HT	:	Hypertension
BCR	:	BUN Creatinine Ratio
CHF	:	Congestive Heart Failure
CVH	:	Cerebrovascular Disease
MV	:	Mechanical Ventilation
HD	:	Hemodialysis

Introduction

Acute Kidney Injury (AKI) is a syndrome that suddenly deteriorates by causing nitrogen accumulation in the body and the fluid-electrolyte imbalance as a result of a sharp decline in glomerular filtration rate. In a study by Mehta et al., they defined AKI as 0.3 mg/dl/h or more increase in creatinine or less than 0.5 mL/kg/h urine output [1].

Acute kidney injury is one of the most worked subjects in nephrology since it causes severe systemic and renal damage. Despite the development of patient care facilities, it is observed in 15% of hospitalized patients and 40% of inpatients at the intensive care unit [2].

To create a common language for AKI, RIFLE (Risk, Injury, Failure, Loss, End-stage kidney disease) classification has been developed by ADQI (Acute Dialysis Quality Initiative) group. With this classification, to talk common language about AKI, to compare studies and studies and to create multinational, multicentered studies were aimed. [3] The crucial issues in this classification is that urine output, creatinine level and glomerular filtration rate as a measure can be used separately. The worst of these values should be taken into consideration. In the studies about RIFLE classification; it was shown that the classification of kidney function and loss was correlated with RIFLE stage. Also, it was proposed that survival prediction property of RIFLE classification was high, and it was guiding in the determination of renal function normalization, continuous renal replacement therapy need, hospital stay duration, mortality, and morbidity [4,5]. AKI diagnosis was made using RIFLE criteria in our study.

Studies demonstrated that; 80% of patients in the ICU are dying of AKI, and 13% need hemodialysis replacement therapy. Despite the development of intensive care standards; because of advanced age, accompanying comorbid situation and invasive interventions made to patients, the risk of development of AKI in intensive care unit patients continues to be a likely possibility [6].

Intensive care patients often need Mechanical Ventilation (MV). In patients requiring MV, Acute Kidney Injury (AKI), develops frequently. Many factors are leading to the AKI. At the same time, even MV alone causes hypotension and disturbs renal perfusion by increasing intrathoracic pressure. In this case, with or without accompanied comorbid factors, medical treatment is insufficient, and renal replacement therapy (hemodialysis) is needed [7].

In our study, we aimed to investigate the risk of developing AKI and related factors depending on mechanical ventilation in 300 patients hospitalized in our anesthesiology and reanimation intensive care unit, between January 1, 2015, and June 31, 2017, who are older than 18 years old, do not have chronic renal failure, did not receive dialysis before and are diagnosed to have AKI based on RIFLE criteria.

Materials and Methods

For our study, the consent was received from Ordu University Clinical Research Ethics Committee (Decision number: 2017/31). File data of hospitalized patients in our intensive care unit between January 1, 2015-31, June 2017 retrospectively. A total of 300 patient's files were examined. For each case, demographic data, hemoglobin, BUN, creatinine, BUN/Creatinine Ratio (BCR), APACHE II score, Glasgow Coma Score (GCS), number of MV days, total hospitalization days, whether to need hemodialysis or not, accompanied comorbid factors were recorded. The patient's discharge status, whether to have exited or not was filed separately for every case. The patients under the age of 18 and those with chronic renal damage previously were excluded from the study.

Statistical Analysis

Statistical analysis was performed using SPSS 17.0 for Windows software (SPSS Inc., Chicago, IL, USA). Data were presented as mean with standard deviance for the numeric variables (age, weight, height, APACHE II score, mechanically ventilation day, hospital stay day), as the number of cases and (%) for categorical variables (COPD, DM, etc.). Univariate logistic regression analysis was performed to assess the main factors associated with hemodialysis performed. Variables in univariate analysis associated with HDP<0.20 in the likelihood ratio test (−2LL) were selected for multivariate logistic regression analyses. All identified individual variables were analyzed with a manual backward elimination procedure starting with a full multivariable logistic regression model. Variables were kept in the model if the -2LL ratio test of the model with and without the variable was significant (p<0.05). Odds Ratio's (OR) are presented with 95% confidence intervals (95% CI). The final individual model was tested with the Hosmer-Lemeshow for the goodness-of-fit test. Additionally, cut off the value of dialysis patients was determined by ROC analysis for APACHE II scores.

Results

The relationship of mean ± standard deviation with mortality is shown in Table 1 according to hemodialysis presence or absence.

As the number of MV days between variables and APACHE II scores increase, the need for hemodialysis also increases (p < 0.001*, p < 0.001*). At the same time, as the average age is increasing also needs for hemodialysis increase (p=0.003α). Also, the need for hemodialysis increases as the duration of hospitalization increases (p = 0.002μ). There was no relationship between the height and weight status of the cases and mortality.

Variables	Hemodialysis Status		P-values
	No	Yes	
Age (year)	70.4 ± 16.	75.7 ± 13.6	0.003$^\alpha$
weight	72.5 ± 14.4	74.2 ±13.3	0.296
height	168.6 ± 11.25	168.47 ± 9.9	0.905
APACHE II score	20.2 ± 11.9	35.39 ± 10.9	<0.001*
MV number of days	1.88 ± 4.04	10.1 ± 7.14	<0.001*
Inpatience time	10.7 ± 10.2	14.2 ± 8.16	0.002$^\mu$

Table 1: Descriptive statistics (mean ± standard deviation) of the examined variables for mortality.

The relationship between potential risk factors and hemodialysis status was assessed with univariate logistic regression analysis. Our results were presented in Table 2.

According to the results of the univariate logistic regression analysis, the risk in individuals to enter dialysis were found as follows. 1.173-fold in women, 1.529-fold in COPD patients, 17.327-fold in sepsis patients, 1.87-fold in DM patients, 5.093-fold in patients with bun creatinine ratio less than 10, 1.46-fold in CHF patients, 1.338-fold in patients with CVD, 131.233-fold higher in MV patients. Six variables were included in the initial multivariate logistic regression model (Excluded four variables according to p >0.20 in the likelihood ratio test: Sex, Hypertension (HT), malnutrition, and Cerebro Vascular Disease (CVD). (Table 2).

Variable	No.	Total No.	Prevalence (%)	B	S.E.	Wald	Sig.	Exp(B)	95%C.I.forExp(B)	
									Lower	Upper
Constant				-4,59	1,005	20,90	<0.001	0.01		
Sex										
male	60	164	36.6							
female	55	136	40.4	,163	,238	,467	,494	1,177	,738	1,878
COPD										
No	44	134	32.8							
Yes	71	166	42.8	,424	,242	3,082	,079	1,529	,952	2,455
SEPSIS										
No	30	189	15.9							
Yes	85	111	76.6	2,852	,300	90,545	<0.001	17,327	9,629	31,179
DM										
No	63	190	33.2							
Yes	52	110	47.3	,592	,245	5,817	,016	1,807	1,117	2,924
HT										
No	46	117	39.3							
Yes	69	183	37.7	-,068	,243	,078	,780	,934	,580	1,504
BUN Creatinine Ratio (BCR)										
High	92	256	35.9							
Low	20	27	74.1	1,628	,458	12,630	<0.001	5,093	2,075	12,500
Malnutrition										
No	100	260	38.5							
Yes	15	40	37.5	-,041	,351	,014	,907	,960	,483	1,909
CHF										
No	40	121	33.1							

Yes	75	179	41.9	,379	,246	2,378	,123	1,460	,902	2,363
CVD									
No	68	190	35.8							
Yes	47	110	42.7	,292	,245	1,415	,234	1,338	,828	2,164
MV									
No	1	100	1							
Yes	114	200	57	4,877	1,015	23,081	<0.001	131,233	17,946	959,681

Table 2: The evaluation results of the relationship between the potential risk factors and hemodialysis status by univariate logistic regression analysis.

Our study strongly suggests that the risk of Hemodialysis (HD) in patients receiving mechanical ventilation has increased significantly. However, a very high correlation with other potential risk factors may be explained by other causes. This can be related with the absence of an intensive care unit for chest diseases in Ordu and in, the presence of many COPD and bronchial asthma cases in the Black Sea region and the fact that our hospital is a third-degree intensive care unit, and we have to follow so many patients with respiratory insufficiency and multiorgan failure.

When the relationship between the potential risk factors and the HD was assessed with multivariate logistic regression analysis, similar results were found with univariate logistic regression analysis. Our results were presented in Table 3.

The final model fit was tested using Hosmer-Lemeshow test. The H-L statistic test has a significance of 0.208 which means that it is not statistically significant and therefore our model is quite a good fit.

Multivariate logistic regression analysis based on the results of the final model, the risk of receiving hemodialysis is 129.76 times higher in mechanical ventilation connection compared to no connection, 2.80 times higher in patients with diabetes compared to nondiabetics, 19.69 times higher in sepsis compared to patients without sepsis, 9.73 times higher in patients with BCR value above 10 compared to under 10 (Table 3).

Variables	B	S.E.	Wald	Sig.	Exp(B)	95% C.I.forExp(B)	
						Lower	Upper
STEP 1[a] (Beginning model)							
Sepsis present	2.9	0.3	90.545	<0.001	17.327	9.629	31.179
Constant	-2	0.199	70.193	<0.001	0.189		
STEP 4 (Final model)							
MV present	4.9	1.05	21.47	<0.001	129.76	16.57	1016.39
DM Present	1	0.4	6.69	0.01	2.8	1.28	6.1
Sepsis present	3	0.4	56.33	<0.001	19.69	9.04	42.89
BUN Creatinine Ratio high	2.3	0.71	10.32	0.001	9.73	2.43	39.01
Constant	-6	1.09	34.53	<0.001	0		
a. Variable(s) entered on step 1: sepsis present							

Table 3: Potential risk factors associated with HD in the multivariate logistic regression equation.

As a result of ROC analysis, dialysis patients' APACHE II scores cut off value was determined approximately as 28, patients with APACHE II score 28 and above the risk of HD increases (Figure 1).
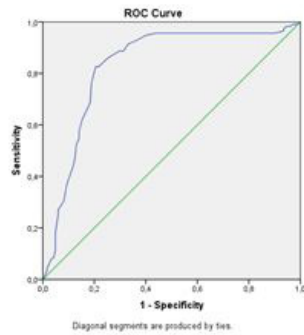
Figure 1: ROC curve showing sensitivity between APACHE II scores of hemodialysis patients was determined as AUC: 0.833 p <0.001 respectively.

Discussion

This retrospective study was planned to examine the incidence of patients with Acute Kidney Injury (AKI) during follow-up at the ICU, relationship with MV, the relationship between co-morbid factors and HD need, and mortality rates.

In a retrospective cross-sectional study conducted by Peres et al. in the same area but in different intensive care units, 7.1% of AKI patients were determined to require HD; in another study by Carmo et al., this rate was found as 12.5%. [8,9]. A possible reason for this incidence discrepancy is that the average age in the studies is different (58/48 years). The literature results are compatible with the results of our research. As the age increased, the need for HD, accompanied by AKI, increased.

The kidneys and lungs are the two most affected organs in the disease called multiple organ failure syndromes. Also, there is some evidence that renal failure affects lung function negatively and this lung injury causes acute renal failure [10]. Hypervolemia, which may occur during renal failure, can increase pulmonary capillary hydrostatic pressure. Cytokines play a significant role in the onset and progression of both AKI and acute lung injury and are seen as the primary factor mediating the local and systemic effects of the renal injury. Feltes et al. found significant associations between the kidney and pulmonary disease in critically ill patients with lung disease [11]. In our study, HD need was increased in patients with respiratory failure who required MV. Our results correspond with those of Feltes et al. Vieira et al. reported that the duration of MV in patients with AKI, the duration of stay in ICU and the rate of ICU mortality were longer when compared to non-AKI patients [12]. The findings of Vieira et al. are similar to our findings. Also in our study, as the number of MV days increased, as the duration of stay in ICU prolonged, HD needs to be increased due to AKI. In this study, no significant difference was found the duration of stay in ICU between patients with and without AKI. However, in our study, as the duration of stay in ICU increases,

AKI risk was found to be significantly increased. Only in this respect, our work is different from the work of Vieira et al.

In a study by Peres et al., mortality was 52% in the AKI group, 62.8% in the study of Abreu et al., and 60.3% in the multicenter study by Uchino et al. [6,13,14] In the case of our research, we found this rate as 57% in AKI cases. Our results correspond with the literature findings. In a multicenter study involving 1449 patients done by Mendonca et al., a significant association was found between chronic heart failure, cardiovascular insufficiency, cirrhosis, respiratory insufficiency, advanced age, and AKI [15]. The results of Mendonca et al. are consistent with our results. Our case number is much lower, being 300 and it is a limiting factor in our study to be carried out from a single center. We also did not follow cirrhotic patients since we did not have gastroenterology specialist. Our results, however, are consistent with the literature, as our study found an increased risk for older age, Congestive Heart Failure (CHF), and HD in patients receiving MV.

In a study involving 514 patients in which Fiaccadori et al. evaluated acute renal failure as a complication of gastrointestinal bleeding, 139 patients experienced hypotension and had a higher rate of acute renal failure [16]. In our study, patients with poor perfusion such as congestive heart failure, had a higher incidence of kidney damage. The animal and human studies have shown that the effects of hyperglycemia and hyperinsulinemia on patients in intensive care unit can lead to AKI by hypoxia, perfusion deterioration, decrease in nitric oxide activity, decrease in synthesis of antioxidant enzymes, increase in free radicals, increase in lipid degradation products, accumulation of excess glucose in kidney tubule cells [17-19].

In Finney SJ's study, intensive care patients with glucose levels <140 mg/dl had a 29% reduction in mortality and 75% reduction in the development of AKI [20]. Wooley JA et al. have shown that hyperglycemic patients with or without Diabetes Mellitus (DM) have a higher incidence of AKI than the control group [21]. In the study by Monson P et al. on intensive care patients receiving Total Parenteral Nutrition (TPN), they demonstrated that the hyperglycemia increased the risk of AKI development [22]. In our study, a significant relationship between the risk of developing AKI and DM in diabetic patients was found. Our results are in accordance with the findings of the literature.

Rangel-Frausto et al. are the first authors to demonstrate that AKI identified with the need of renal replacement treatment was increased significantly according to the presence of sepsis (24%), severe sepsis (39%) or septic shock (89%) [23]. Lopes et al. showed that when classification from severe sepsis to septic shock was done, the rate of AKI was increased from 29% to 51% [24]. Lopes et al.'s work determined that severity of AKI in septic shock was relatively worse and most of them were in failure category of RIFLE compared to those of undergoing severe sepsis (36% versus 64%).

They alleged that physiopathologic differences in AKI caused by sepsis and other etiologies (ischemia, toxin, cardiopulmonary bypass) play an essential role in determining early renal injury, changes in renal function, and the direction of AKI and early detection of renal injury. The results of Lopes and Rangel-Frausto et al. is in harmony with our results. In our study, we detected that AKI incidence requiring HD replacement therapy in sepsis patients was very high.

AKI is a disease that is common and with high disease burden. It is a disease with more anomalies and higher laboratory parameters compared to AKI without sepsis or only sepsis. Also, we showed that septic AKI caused an important and independent increase regarding hospital mortality, compared to non-septic AKI or sepsis. Septic AKI in surviving patients resulted in an increase in the ICU and hospital stay duration and also in prolongation of discharge possibility from rehabilitation or another acute care facility. We claim that these data support the concept of which septic AKI can represent a unique pathophysiological state. Moreover, in future studies, potential therapeutic interventions could be possible with considering these differences in AKI pathophysiology [25]. In our study, we had high mortality rates in cases with sepsis and AKI co-occurrence. Infection rates of the intensive care unit of our hospital were high, and the vast majority of the cases died due to septic shock. As in the study of Bagshaw et al., in our study; this situation explains the high mortality rates in patients with sepsis and AKI combination and with non-septic AKI. Our results coincide with the findings of the literature.

In Soares de Abreu et al.'s study; in AKI and Acute Respiratory Distress (ARDS) diagnosed patients taking MV in intensive care " How is the interaction of lung and kidney? " study while the higher mortality in patients with AKI in ICU was found, in the same study there was no relationship between MV and AKI [13]. Soares de Abreu et al.'s study results contradict with our work in terms of MV - AKI. In the same study, the authors found the cut off value as 20 for APACHE II score in the ROC curve drawn for the relationship between APACHE II score AKI. In our study, we found the cut off value as 28 for the same relation. Soares de Abreu et al. did a prospective study with 100 cases. Our study is a retrospective study involving 300 cases. Although our case number is higher compared to the work of Soares de Abreu et al., being a retrospective study is one of the factors of our work to be restrictive. We believe that our cut off value reflects reality for our region; however, there is a need for long-running prospective ICU study about this case with a larger number of cases.

As a result; the possibility of the development of AKI in intensive care patients is high. In cases connected to a mechanical ventilator, AKI development was more likely, and hemodialysis need is the inevitable result. Therefore, non-invasive mechanical ventilation therapy should be tried first in appropriate indications in cases requiring mechanical ventilation to reduce the development of AKI in ICUs; invasive mechanical ventilation should be tried at a later time. Besides, to reduce the possibility of development of AKI, advanced monitorization techniques should be used more.

Conclusion

To reduce the incidence of AKI depending on mechanical ventilation, non-invasive mechanical ventilation, advanced monitorization facilities should be present for each intensive care unit.

Ethics Committee Approval: Clinical Studies Ethics Committee of Ordu University, Faculty of Medicine, January 2017; Decision Number: 2017/31.

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