Predictors of Acute Kidney Injury in Patients with High-degree Atrioventricular Block

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ABSTRACT

Introduction: This study aimed to investigate the predictors of acute kidney injury (AKI) in patients with high-degree atrioventricular (AV) block. To the best of our knowledge, this is the first study to examine the relationship between high-degree AV block and AKI in coronary intensive care unit (ICU).

Patients and Methods: In this retrospective study, 226 patients who were admitted to the coronary ICU of our hospital and diagnosed as high-degree AV block were included. AKI was evaluated according to Acute Kidney Injury Network criteria. Logistic regression analyses were performed to identify the independent predictors of AKI in patients with high-degree AV block.

Results: Patients with high-degree AV block were divided into two groups as with or without AKI. Mean age of the patients was 73 ± 14.61, and 50% of the patients were female. AKI was observed in 34% of the coronary ICU with high-degree AV block. In the present study, in-hospital mortality was 6.2% (n= 14) in all patients. In multivariate analyses, eGFR (OR: 0.944, 95% CI: 0.927-0.960; p< 0.001) and LVEF (OR: 0.952, 95% CI: 0.925-0.980; p< 0.001) were found to be independent predictors of AKI in high-degree AV block patients.

Conclusion: Our study, in which AKI was evaluated in high-degree AV block patients, revealed the frequency and predictors of AKI development in high-degree AV block patients for the first time. We found that reduced LVEF and decreased eGFR were independent predictors of AKI in high-degree AV block patients.

Key Words: High-degree atrioventricular block; acute kidney injury; left ventricular ejection fraction

Yüksek Dereceli Atriyoventriküler Blok ile Başvuran Hastalarda Akut Böbrek Hasarı Öngördürücüleri

ÖZET

Giriş: Bu çalışmada yüksek dereceli atriyoventriküler (AV) blok ile koroner yoğun bakıma yatırılmış hastalarda akut böbrek hasarı (ABH) gelişiminin öngördürücülerinin incelenmesi amaçlanmıştır. Bizim bilgilerimize göre yapmış olduğumuz bu çalışma, atriyoventriküler blok ile akut böbrek hasarı arasındaki ilişkiyi inceleyen ilk çalışmadır.

Hastalar ve Yöntem: Bu retrospektif çalışmaya yüksek dereceli AV blok ile koroner yoğun bakım ünitesine yatırılan 226 hasta dahil edildi. Hastalarda akut böbrek hasarı "Acute Kidney Injury Network" kriterlerine göre tanımlandı. AV blok hastalarında ABH'nın bağımsız öngördürücüleri lojistik regresyon analizi ile tespit edildi.

Bulgular: Yüksek dereceli AV blok tanısı ile takip edilen hastalar ABH gelişip gelişmemesine göre iki gruba ayrıldı. Hastaların ortalama yaşı 73 ± 14.61 idi ve hastaların %50'si kadındı. Takipte tüm hastaların %34'ünde ABH geliştiği gözlendi. Çalışmaya dahil edilen tüm hastalarda hastane içi mortalite oranı %6.2 (n= 14) olarak tespit edildi. Lojistik regresyon analizinde tahmini glomerüler filtrasyon hızı (OR: 0.944, 95%CI: 0.927-0.960; p< 0.001), sol ventriküler ejeksiyon fraksiyonu (OR:0.952, 95%CI: 0.925-0.980; p< 0.001) ABH'nın bağımsız prediktörleri olarak bulundu.

Sonuç: Bu çalışmada, literatürde ilk defa yüksek dereceli AV blok hastalarında ABH'nın olası öngördürücüleri ve sıklığı değerlendirildi. Düşük LVEF ve azalmış eGFR'nin, yüksek dereceli AV blok hastalarında AKI'nın bağımsız öngördürücülerinden olduğunu saptadık.

Anahtar Kelimeler: Yüksek dereceli atrioventriküler blok; akut böbrek hasarı; sol ventrikül ejeksiyon fraksiyonu

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INTRODUCTION

Acute kidney injury (AKI), usually occurring within hours and days, is a potentially reversible decrease in the kidney's capacity with the retention of nitrogenous waste products and creatinine and reduction in the capacity of maintaining fluid and electrolyte homeostasis[1]. AKI has a frequency of 3-7% in hospitalized patients and a frequency of 3.2-78 % in intensive care unit (ICU) patients[2-4]. The most common causes of AKI are decreased kidney perfusion, drugs, radiocontrast exposure, postoperative period, and sepsis[5]. AKI is associated with significantly increased mortality, hospital stay, and burden[4].

Atrioventricular (AV) block is a disorder that occurs with the disturbance of electrical conduction, which can be permanent and temporary[6]. The risk of hemodynamic instability in hospitalized patients with AV conduction delay is already high. Therefore, the emergence of additional comorbid conditions to hemodynamic instability makes it much more difficult to handle these patients[7].

The functions of the heart and kidney are in an inseparable relationship. The kidneys receive 20-25% of the cardiac output per cycle[6]. Therefore, some cardiac disorders may lead to the development of AKI by causing decreased renal perfusion[8]. The development of AKI is accelerated with the reduction of cardiac output in patients with bradycardia[9].

Both AV blocks and AKI are conditions with high mortality and morbidity[7,10]. Therefore, early diagnosis and treatment is important in this patient group. This study aimed to investigate predictors of AKI in patients with high-degree AV block.

PATIENTS and METHODS

Study Population

In this retrospective study, 226 patients who were admitted to the coronary care unit of our institution (Dr. Siyami Ersek Thoracic and Cardiovascular Surgery Training and Research Hospital) between 2013 and January 2016 and diagnosed as high-degree AV block were included. Demographic and clinical data, laboratory tests and electrocardiography (ECG) recordings were retrospectively recruited from the hospital registry system. The study protocol was reviewed and approved by the local ethics committee of the hospital.

Echocardiographic Examination

Echocardiographic examinations of the patients included in the study were performed with Vivid 3 ultrasound system (GE Vingmed Ultrasound, Horten, Norway) using the standard imaging techniques recommended by the American Society of Echocardiography. Continuous single lead ECG was obtained from each participant during echocardiography. Left ventricle ejection fraction (LVEF) was calculated by Simpson's method.

Electrocardiographic and Laboratory Analysis

Digital 12-lead standard ECGs with a paper speed of 25 mm/s and 10 mm/mV had been performed on each patient. ECGs, which were taken in the emergency room during hospital admission, were recorded in the patient file along with the patient's barcode and dates. All ECG evaluations were made by two experienced cardiologists, taking account of the opinion of a third cardiologist in case of disagreement. Patients with high-degree AV block were included in the study. High-degree AV block is defined as the presence of Mobitz type II second-degree or third-degree AV block[11,12].

The estimated glomerular filtration rate (eGFR) values of the patients were calculated using the Modification of Diet in Renal Disease (MDRD) formula. AKI was evaluated according to Acute Kidney Injury Network (AKIN) criteria[13].

Statistical Analysis

Statistical analyses were performed using NCSS (Number Cruncher Statistical System) 2007 (Kaysville, Utah, USA). Normality of the data was analyzed using the Kolmogorov-Smirnov test. The numerical variables with a normal distribution are presented in terms of mean ± standard deviation (SD) values, while the non-normally distributed variables are presented as median and interquartile range values. Frequencies were calculated for the categorical variables (numbers and percentages [%]). Continuous variables of both groups were compared using the Student's t test or the Mann Whitney U test. Categorical data were compared using the Chi-square test or Fisher's exact test. Statistical significance was defined as a p value of < 0.05. Correlations between continuous variables were assessed using the Pearson correlation coefficient for variables with normal distribution and Spearman's rank correlation coefficient for variables without normal distribution. Logistic regression analyses were performed to identify the independent predictors of AKI in patients with high-degree AV block. The survival curve was calculated using the Kaplan-Meier method, and a log-rank test was used to compare the difference in survival between the groups.

RESULTS

A total of 226 patients (mean age 73 ± 14.61 years, 50% female) with high-degree AV block were divided into two groups according to the occurrence of AKI. Baseline demographics, clinical characteristics and laboratory parameters of the patients are listed in Table 1. AKI was observed in 34% of the coronary ICU patients with high-degree AV block. There were no statistically significant differences between the groups in terms of age, sex, smoking, hypertension (HT), and congestive heart failure (CHF). Diabetes mellitus (DM) and history of coronary artery disease (CAD) were higher in patients with AKI.

Table 1. Demographic, clinical and laboratory characteristics of all patients with and without acute kidney injury

	All patients; n: 226		AKI (-); n: 148		AKI (+); n: 78		p
Age; years	73	±4.61	72	±15.03	74	±13.84	0.767
Female gender; n (%)	113	50	69	46.6	44	56.4	0.163
Smoking; n (%)	21	9.3	12	8.1	9	11.5	0.399
Hypertension; n (%)	145	64.2	90	60.8	55	70.5	0.149
Diabetes Mellitus; n (%)	67	29.6	35	23.6	32	41	0.007
CAD; n (%)	22	9.7	10	6.8	12	15.4	0.038
CHF; n (%)	44	19.5	24	16.2	20	25.6	0.090
History of valve surgery; n (%)	13	5.8	7	4.7	6	7.7	0.364
History of CVD; n (%)	31	13.7	16	10.8	15	19.2	0.081
Beta blocker; n (%)	61	27	34	23	27	34.6	0.061
Calcium channel blocker; n (%)	11	4.9	7	4.7	4	5.1	0.895
Digoxin; n (%)	7	3.1	6	4.1	1	1.3	0.254
Mad honey intoxication; n (%)	4	1.8	2	1.4	2	2.6	0.512
Heart Rate;/min	41.49	±9.84	41.43	±9.63	41.60	±10.27	0.667
SBP; mmHg	139.67	±25.73	141.22	±26.05	136.73	±25.01	0.270
DBP; mmHg	65.11	±14.27	65.26	±13.41	64.82	±15.86	0.864
Sodium; mmol/L	137.75	±5.06	138.37	±4.76	136.56	±5.43	0.003
Potassium; mmol/L	4.66	±0.75	4.52	±0.63	4.93	±0.89	0.000
Peak creatinine; mg/dL	1.10	(0.83-1.64)	0.92	(0.77-1.17)	1.73	(1.29-2.28)	0.000
Creatinine on admission; mg/dL	1.07	(0.84-1.50)	0.91	(0.78-1.15)	1.53	(1.21-2.02)	0.000
eGFR on admission; ml/min	58.31	±27.61	69.21	±24.22	37.64	±21.13	0.000
Hemoglobin; g/dL	12.08	±1.75	12.21	±1.68	11.84	±1.87	0.180
Acute Respiratory Failure;							
NPPV; n (%)	3	1.3	2	1.4	1	1.3	0.590
IV; n (%)	9	4	5	3.4	4	5.1	
Acute renal failure complication; n (%)	18	8	5	3.4	13	16.7	0.000
Temporary pacemaker usage; n (%)	45	19.9	22	14.9	23	29.5	0.010
Permanent pacemaker usage; n (%)	169	74.8	115	77.7	54	69.2	0.160
Left ventricle ejection fraction; %	51.33	±11.96	52.81	±11.47	48.88	±12.46	0.048
Duration of hospitalization; days	6	(4-8)	7.00	(5-10)	6	(4-10)	
In-hospital mortality; n (%)	14	6.2	8	5.4	6	7.7	0.934

Abbreviations: AF: Atrial fibrillation, AKI: Acute kidney injury, AV: Atrioventricular, CAD: Coronary artery disease, CHF: Congestive heart failure, CVD: Cerebrovascular disease, DBP: Diastolic blood pressure, eGFR: Estimated glomerular filtration rate, IV: Invasive ventilation, NPPV: Noninvasive positive pressure ventilation, SBP: Systolic blood pressure.

Heart rate, systolic and diastolic blood pressures of the patients were similar in both groups. In the AKI group, laboratory findings demonstrated that while sodium level was lower, potassium and creatinine levels were significantly higher. In both groups, medications (beta-blockers, calcium channel blockers, digoxin) and history of mad honey intoxication were similar. LVEF was significantly lower in the group of patients with AKI than the group of patients without AKI (LVEF, 48.88 ± 12.46 vs. 52.81 ± 11.47, p= 0.048). The rate of temporary pacemaker implantation was higher in the patients with AKI. In our study

Table 2. Univariate and multivariate logistic regression analysis of acute kidney injury predictors in patients with high-degree atrioventricular block

	Univariate analysis			Multivariate analysis		
	Odds ratio	95% CI	p	Odds ratio	95% CI	p
eGFR	0.939	0.923-0.956	< 0.001	0.944	0.927-0.960	< 0.001
LVEF	0.938	0.915-0.961	< 0.001	0.952	0.925-0.980	0.001

Abbreviations; CI: Confidence interval, eGFR: Estimated glomerular filtration, LVEF: Left ventricle ejection fraction.

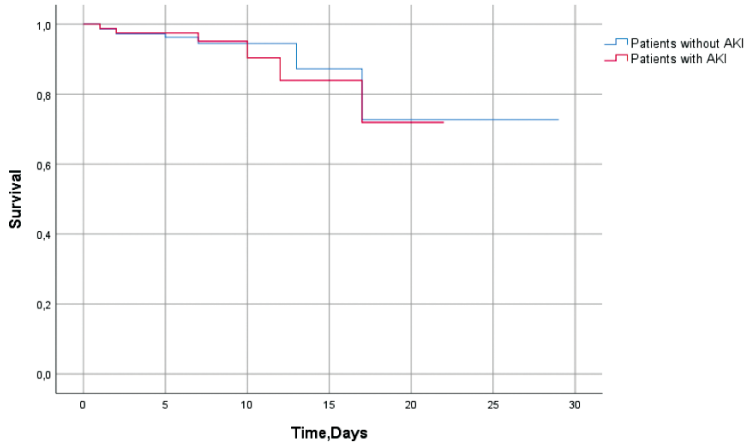

Figure 1. Kaplan-Meier survival curve for in-hospital mortality in patients with and without acute kidney injury.

population, the rate of permanent pacemaker implantation was 74.8% (n:169), while it was 69.2% (n: 54) in patients with AKI and 77.7% (n: 115) in patients without AKI. The median hospital stay of all patients was 6 (4-8) days. Total in-hospital mortality rate was 6.2% (n: 14) and 7.7% (n: 6) in the AKI group. The median follow-up time in all patients who died was 6 (1.75-12.25) days, while in other patients, it was 6 (4-8) days.

The parameters found to be associated with AKI in univariate analysis (eGFR on admission, DM, history of CAD, LVEF), history of cerebrovascular disease and hemoglobin were adjusted in logistic regression to identify the independent predictors of AKI. In multivariate analyses, eGFR (OR: 0.944, 95% CI: 0.927-0.960; p< 0.001) and LVEF (OR: 0.952, 95%CI: 0.925-0.980; p< 0.001) were found to be independent predictors of AKI (Table 2).

Although it is not statistically significant, Kaplan-Meier survival analysis showed that patients with AKI had a higher death rate than those without AKI (Figure 1).

DISCUSSION

In our study, we investigated the predictors of AKI in high-degree AV blocks and found out that reduced LVEF and decreased eGFR on admission were independent predictors of AKI in high-degree AV block patients in the coronary ICU. The mortality rate was 6.2% in patients admitted to the coronary ICU with high-degree AV block regardless of AKI occurrence. To the best of our knowledge, this is the first study examining the predictor of AKI in high-degree AV block patients.

Acute kidney injury, which usually occurs with a reversible decrease in renal function, is an important cause of mortality, morbidity, and increased length of stay in ICU patients. According to the underlying disease, the incidence of AKI in the ICU ranges from 3.2% to 78%[2]. High-degree AV block is an important cardiac conduction disorder mostly treated with a permanent pacemaker[14]. In many studies, although hypoperfusion resulting from various diseases has been shown to impair the functions of the kidney, the effect of the presence of high-degree AV block on AKI development in patients has not been shown yet[8]. In our study, AKI was observed in 34% of coronary ICU patients with high-degree AV block. This rate does not seem to be low when AKI rates in other diseases frequently seen in the ICU are considered (i.e. 42% in sepsis patients[11], 18% in STEMI patients[15], 20.9% in patients with cerebrovascular disease[16].

Many diseases, including DM, CAD, CHF, HT, and basal kidney dysfunction, have been demonstrated to be common in ICU patients who develop AKI[17]. In parallel with previ-

ous studies, it was observed that decreased eGFR and CAD were higher in patients who developed AKI in high-degree AV block patients. Similarly, DM was more common in patients with high-degree AV block in our study. In diabetic patients, the presence of subclinical renal injury could facilitate the development of AKI[18].

Several studies investigating demographic, clinical, biochemical, and hematological parameters have been conducted to find out the independent predictors of AKI in intensive care patients[2,19,20]. Although advanced age, reduced LVEF, anemia, and decreased renal function have been reported as independent predictors for AKI in previous studies, independent predictors for AKI in high-degree AV block patients have not been studied yet[21,22]. In our study, reduced LVEF and decreased eGFR on admission were found as independent predictors of AKI. Left ventricular systolic dysfunction is known to cause both reduced cardiac output (CO) and elevated LV filling pressures[23]. Bradyarrhythmia can also cause reduced CO[24]. Cardiac output is calculated by multiplying stroke volume and heart rate[25]. In patients with decreased LVEF, the reduction in stroke volume is compensated by various neurohormonal mechanisms during the chronic process of the disease[6]. The development of sudden bradycardia in these patients may lead to a sudden decrease in cardiac output and cause acute decompensation. Therefore, it might cause impaired renal perfusion and the development of AKI[9].

Although it is not clear why decreased eGFR is a predictor for AKI, previous studies have shown that the risk of AKI increases with decreased eGFR below 60 ml/min/1.73m^2[17,26]. It has been speculated that the development of AKI may be associated with the failure of damaged kidneys to overcome with triggering factors such as decreased kidney reserve and hypoperfusion or nephrotoxic drugs in patients with decreased eGFR[27]. Similarly, in our study, decreased eGFR on hospital admission was found to be a predictor for AKI.

In patients with AKI, acute deterioration in renal function could cause electrolyte imbalance, acid-base disturbance, and volume overload. This acute imbalance in the hemodynamics of patients could lead to increased mortality and morbidity in these patients[28]. In our study, the average length of hospital stay in patient with AKI was six days, and six of these patients (7.7%) died in-hospital. Although it did not reach statistical significance, the mortality rate in patients with AKI was higher than those without AKI.

Our study has some limitations. First, it was a retrospective study with a relatively small sample size. Second, since long-term follow-up of the patients did not exist in our data, information on long-term mortality could not be introduced. Third, subjects included in this study could not represent a homogeneous group since patients with a history of various cardiovascular, cerebrovascular diseases, and patients taking different medications were included in the same study. Finally, we had no information about the effect of AKI on long-term kidney function in our patients.

Our study, in which AKI was evaluated in high-degree AV block patients, revealed the frequency and the predictors of AKI development in high-degree AV block patients for the first time. We found that reduced LVEF and decreased eGFR, which are known as predictors of AKI in other clinical disorders, are independent predictors of AKI in high-degree AV block patients.

Ethics Committee Approval: The approval for this study was obtained from Dr. Siyami Ersek Thoracic and Cardiovascular Surgery Training and Research Hospital Ethics Committee (Decision no: 280011928-051-99 Date: 10.05.2017).

Informed Consent: This is retrospective study, we could not obtain written informed consent from the participants.

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