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Serum Potassium Levels at Admission as a Predictor of Major Adverse Cardiovascular Outcomes in Hospital and 30 Days after Discharge in Acute Heart Failure Patients

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Abstract : Background: Acute Heart Failure (AHF) is still a problem in the world, with mortality and morbidity rates in patients with acute HF are still high. Prognosis estimation in acute heart failure patients still develops. Serum potassium levels can be used asa predictor in patients with acute heart failure. Low and high potassium levels are often a problem in the treatment of patients with acute heart failure. This study aims to determine whether potassium can be used as a predictor of major cardiovascular events (MACE) in patients with acute heart failure. **Method:** This study is a prospective cohort study of 94 patients with acute heart failure treated in Haji Adam Malik General Hospital from August 2017 to February 2018. The cut off point of potassium levels was determined by using ROC curve, then bivariate and multivariate analysis were applied to determine predictor of in hospital major cardiovascular events and 30 days post discharge. Kaplan Meier's survival test was performed to assess survival rate.
Result: From 94 subjects, 36 (38.3%) subjects experienced MACE during treatment in hospital. Subjects with arrhythmias during treatment were 5 people (5.3%) and 28 people (29.8%) deadin this study. From the ROC curve, potassium cut off level was 4.45 mEq/L. According to bivariate analysis, age, sex, osmolality, blood urea nitrogen, blood sugar, potassium, creatinine, and ejection fraction were significant as MACE predictors. From multivariate analysis, potassium ≥ 4.45 mEq/L was a predictor of MACE during treatment in hospital (p = 0,000 OR 8.201 CI 95%: 2.557-26.301) along with age and creatinine. The survival test showed a relative risk of death 3.05 times in potassium ≥ 4.45 mEq/L.
Conclusion: The potassium level at admission was significant to predict in hospital MACE in acute heart failure, but not a good predictor for 30 days after discharge.
Keywords : Serum Potassium level, Acute Heart Failure, MACE.

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Introduction

Acute Heart Failure (AHF) is still a major problem in the world, with mortality and morbidity rates are still high. Life expectancy rate of patients with heart failure is still low, 17-45% of hospitalized heart failure patients will die within a year after being treated[1].

The American Heart Association (AHA) Guidelines for the Management of Heart Failure 2017 describes biomarkers as parameters in the prognosis of acute heart failure patients such as peptide natriuresis, ST2 Soluble Receptor, galactein-3 and troponin[2]. But ironically, not all of these biomarkers are available, not even routinely done because it deals with issues of financing and health insurance.

Potassium levels can be one of the predictors in acute heart failure patients. In patients with acute heart failure, the pathophysiology of the disease, the mechanism of the renin-angiotensin-aldosterone system (RAAS), the effects of treatment and some comorbids may result in the condition of diskalemia, which can be fatal if undetected and corrected[3].

Research on potassium levels is still growing and even between several studies still have contrasting results[4,5,6,7,8]. These results between one study and another provide a confusion in the prognostic value of potassium levels in patients with acute heart failure. Meanwhile, the clinical guidelines recommend to maintain potassium levels at 4.5 to 5.5 mmol / l, but this is still confusing between the various studies[1,9].

Methods

This study was a prospective cohort in which prospective sampling, which tested serum potassium levels at hospital admission as a predictor of major cardiovascular events (MACE) during treated in hospital and 30 days post discharge in acute heart failure patients . Data was taken from the medical record of acute heart failure patients who were admitted to Haji Adam Malik Medan Hospital from August 2017, followed prospectively during treatments and 30 days after discharge.

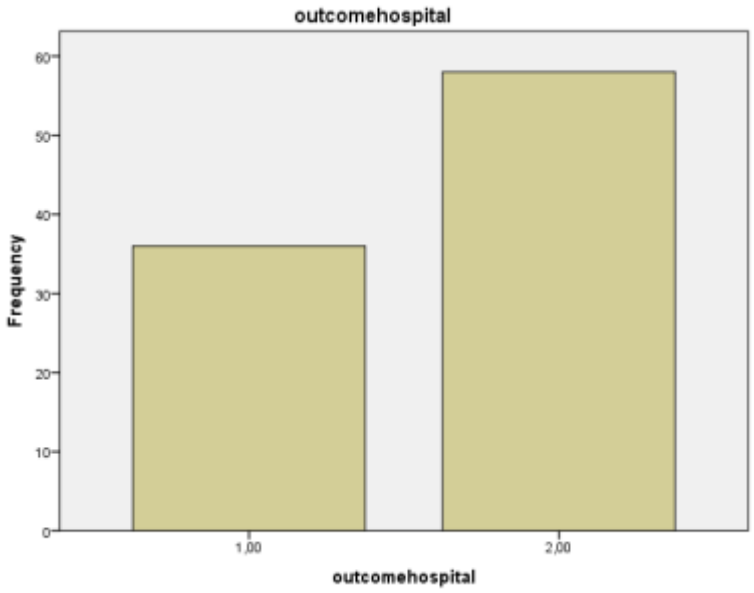
The inclusion criteria were patients diagnosed with acute heart failure based on European Society Cardiology (ESC) Guidelines of Acute Heart Failure 2016 and had complete medical record data. Exclusion criteria were patients with acute heart failure with comorbid shock except cardiogenic shock, patients with adrenal gland disorders, rhabdomyolysis and have advanced malignancies.

Examination of serum potassium levels was taken when the patient admitted to hospital through Clinical Pathology Laboratory of Haji Adam Malik Hospital Medan.Major adverse cardiovascular outcomes (MACE) were observed during treatment in hospital and 30 days after discharge. Major cardiovascular events in the treatment were death and arrhythmia. It is observed continuously through medical record and observation directly. Meanwhile, major cardiovascular events 30 days after discharge were observed by direct telephone communication to the family or patients comprehensively. The observed conditions were death and rehospitalization.

The numerical data was presented with the mean +/- standard deviation or median value. The categorical data was presented by frequency and percentage. Bivariate analyzes were performed with Student's T-test or Mann Whitney test on numerical variables, Chi-square or Fischer test on categorical variables. Multivariate analysis used logistic regression with backward stepwise method. A survival test for 30-day mortality was presented with Kaplan-Meier chart.

Results

Total number of study subjects was 94 people. From 94 study subjects, there were 36 (38.3%) acute heart failure patients with major cardiovascular events during treatments in hospital. Meanwhile, 58 (61.7%) subjects did not experience major cardiovascular events during hospitalization (Figure 1).



1= MACE (+) 2= MACE (-)

Figure 1. Major Cardiovascular Adverse Events during Treatment in Hospital

From subjects who experienced major cardiovascular events during hospitalization, subjects experienced arrhythmias during treatment in hospital were 5 (5.3%), while those who died during hospital stay were 28 (29.8%). 3 people (3.2%) had arrhythmias and died during hospitalization.

The mean age of the subjects was 58 years. The average potassium levels of all patients were 4.39 mEq/l. Mean rate of potassium levels from subjects with major cardiovascular events was 4.84 mEq/l and 4,122 mEq/l for those who did not. Mean creatinine levels was 1.5 mg/dl in all study subjects (Table 1).

Table 1.Clinical characteristic and demography

Characteristics	**Patients n :94 (100%)**	**MACE**		***P* value**
		(+) n : 36 (38.3%)	**(-) n: 58 (61.7%)**	
Age (mean), years	57.86 ± 9.74	60.19±11.53	56.41±8.22	0.067*
Male	71(75.5%)	24(33.8%)	47(66.2%)	0.093[#]
Female	23(24.5%)	12(52.1%)	11(47.8%)	0.132[#]
Systolic (mmHg)	120 (60-260)	90 (60-220)	130 (70-260)	**0.000[b]**
Diastolic (mmHg)	80 (20-140)	60 (20-120)	100 (60-140)	**0.000[b]**
Heart Rate (x/i)	110 (66-150)	120 (66-150)	100 (70-149)	**0.000[b]**
Hemoglobin (g/dL)	13.64 ± 2.10	13.33 ± 1.81	13.83 ± 2.25	0.246*
BUN (mg/dL)	25.37 (66-88)	28.56 (11.52-88)	26.27 (9.13-84)	**0.023[b]**
Blood Glucose (mg/dL)	143.5 (66-481)	140.5 (66-414)	148.5 (84-481)	0.325[b]
Sodium (mEq/L)	133.53 ± 5.37	132.69 ± 6.04	134.05± 4.90	0.261*
Potassium (mEq/L)	4.39 ± 0.806	4.84 ± 0.77	4.122 ± 0.70	**0.000***
Chloride (mEq/L)	103 (85-115)	101 (93-113)	103 (85-115)	0.233[b]
Osmolality (mOsm/L)	301.68(80.84-324)	298(80.84-321.7)	302.9 (80.84-324)	0.457[b]
Creatinine (mg/dL)	1.5 (0.61-7.22)	2.48(0.61-7.22)	1.26(0.63-4.51)	**0.002[b]**
Ejection Fraction (%)	36.17 ± 9.64	32.58 ± 7.55	38.39± 10.17	**0.002***

The cut-off points from serum potassium levels at admission was determined by using ROC curve, then using under the curve (AUC) area to assess the prognostic factor.From the ROC curve, the cut-off serum potassium levels at the admission was 4.45 meq/L with 64% sensitivity and 75% specificity (Figure 2).

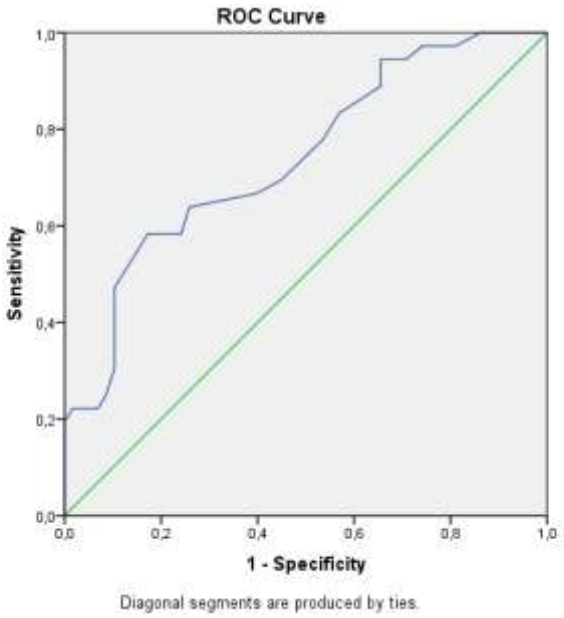


Figure 2. ROC Curve Cut-Off Points of Potassium Level at admisson against MACE

From the results of bivariate and multivariate analysis, the variables that have a prognostic value were potassium (OR 8.201 [95% CI 2.557-26.301]; p <0.05), creatinine (OR 5.016 [95% CI 1.422-17.699]; p <0.05) and age (OR 4.880 [95% CI 1.182-20.144]; p < 0.05) (Table 2).

Table 2. Multivariate analysis of MACE predictors

	Variables	**Coefficient**	**P**	**OR (95% CI)**
	Potassium	2.104	**0.000**	8.201 (2.557-26.301)
	EF	1.021	0.073	2.777 (0.910-8.473)
	Creatinine	1.613	**0.012**	5.016 (1.422-17.699)
	Osmolality	-0.897	0.115	0.408 (0.134-1.245)
	Age	1.585	**0.028**	4.880 (1.182-20.144)
		-1.335	0.152	0.263

Table 3. Analysis of Potassium against 30 days MACE after discharge

Variable		**30 days MACE (+) N = 5 (7.9%)**	**30 days MACE (-) N = 58 (92.1%)**	**P value**
Potassium	≥ 4.45 mEq/L	2 (11.1%)	16 (88.9%)	0.618 *
	< 4.45 mEq/L	3 (6.7%)	42 (93.3%)	
Total		5 (7.9%)	58 (92.1%)	

From 63 subjects followed for 30 days, 5 (7.9%) subjects had MACE and 58 (92.1%) subjects did not experience MACE. A total of 2 (11.1%) subjects had potassium levels ≥ 4.45 mEq/L and 3 (6.7%) had potassium levels <4.45 mEq/L.From 2 subjects who had MACE and had potassium levels ≥ 4.45 mEq/L, 1 (5.6%) subject got rehospitalized and 1 (5.6%) subject died.From analysis of serum potassium levels against 30-day MACE, it was found that potassium level was not statistically significant as a predictor (p=0.618) (Table 3).

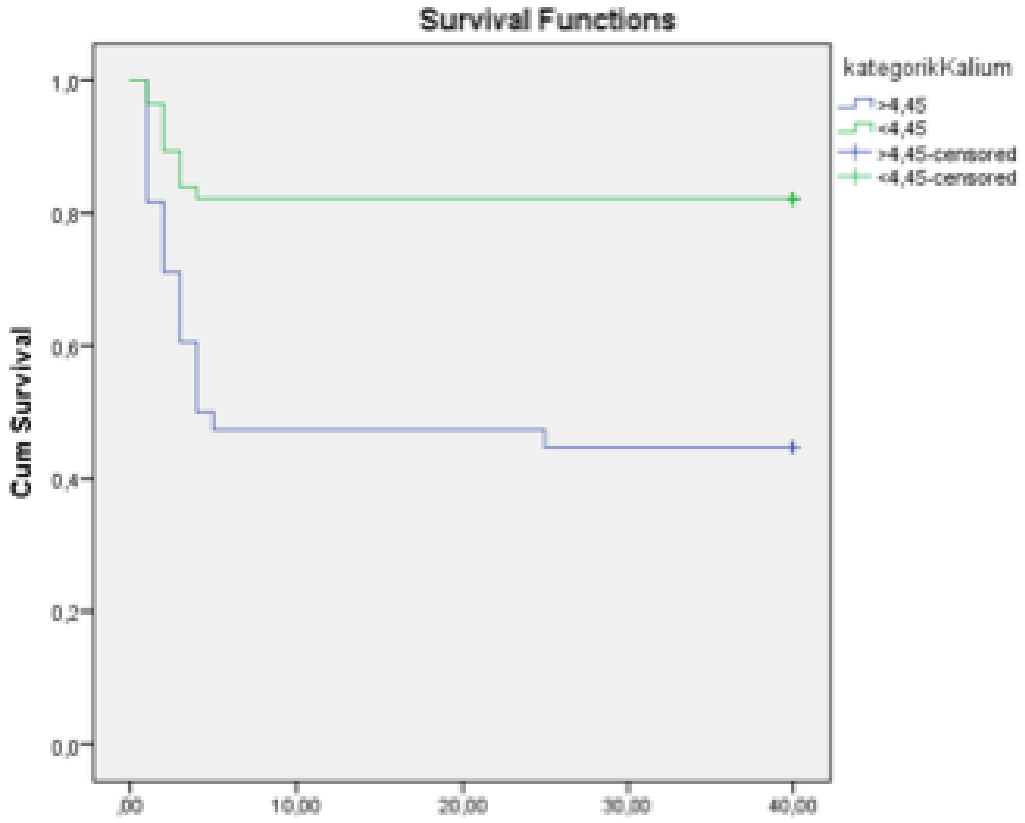


Figure 3. Survival testof potassium level

The survival test was performed using Kaplan Meier curve. On this Kaplan Meier curve it was found that, in patients with potassium levels <4.45 mEq/L had a higher survival rate on the first day of care until 30 days of follow-up (Figure 3). At 10 days, for example, potassium levels <4.45 mEq/L survival rate was 80%, while on potassium ≥ 4.45 mEq/L was 45%. The incidence of death was 55% at subjects with potassium ≥ 4.45 mEq/L while <4.45 mEq/L was 18%. It can be interpreted that relative risk of death incidence (RR) 3.05 times at potassium levels ≥ 4.45 mEq/L compared to patients with potassium level <4.45 mEq/L. When looking at hazard ratio the death incidence was 5.094 times in patients with potassium ≥ 4.45 mEq/L.

Discussion

The study was conducted in the Haji Adam Malik Hospital from August 2017 with sample collection looking at the medical records of patients with acute heart failure in emergency room care, Cardiovascular Care Unit (CVCU) and in-room care. From 94 study subjects, there were 36 (38.3%) subjects with major cardiovascular events during both death and arrhythmia in hospital. From this study showed that potassium levels can be used as a predictor of death and arrhythmia events during treatment in hospital in patients with acute heart failure. In addition to potassium, creatinine and age values also turned out to be predictors of MACE during treatment in acute heart failure patients.

This is in accordance with previous studies by Tromp et al where it was found that potassium levels at hospital admission may be a predictor of mortality in acute heart failure after univariate analysis[7]. In this study it was found that in patients with potassium levels above 4.45 mEq/L found elevated creatinine levels, but not statistically significant. It is also suggested by Tromp et al, where it is said that hyperkalemia does not fully describe the condition of kidney function, even subjects with high potassium have a better diuretic response[7].

In this study also found the relative risk of mortality (RR) was 3.05 times on potassium levels ≥ 4.45 mEq/L than patients with potassium <4.45 mEq/L. When looking at hazard ratio the death incidence 5.094 times in patients with potassium ≥ 4.45 mEq/L. This result is different from Khan et al who suggested that potassium value was not associated with clinical outcomes[10]. This difference may be due to the previous study,

populations taken to be limited only to patients with impaired systolic function, in contrast to this study which took the population of acute heart failure with both normal and low ejection fractions[10].

The results was also in accordance with previous studies, which obtained potassium levels above 4.5 mEq/L associated with the risk of death[11]. This study found potassium levels of 4.45 mEq/L can be used as a predictor of death and arrhythmia during the period of treatment. In the study Bowling et al said that low potassium levels associated with increased mortality. These results differ from this study where patients with potassium levels of 4.45 mEq/L have a greater incidence of death compared to patients with potassium < 4.45 mEq/L. This difference may be due to differences in sample populations where in the previous study populations were entered only with aged > 65 years and divided into 2 groups, the hypokalemia group and normokalemia[11].

From 63 patients followed for 30 days, 5 (7.9%) patients had MACE and 58 (92.1%) did not experience MACE. A total of 2 (11.1%) patients had potassium levels of 4.45 mEq/L and 3 (6.7%) had potassium levels <4.45 mEq/L. From these results, in this study the potassium level was not significant as a predictor of MACE 30 days after discharge. This is also in accordance with the results of previous studies suggesting that potassium is not significant as a predictor of mortality and rehospitalization after 30 days[7].

Serum potassium level at admission is a predictor for major cardiovascular events during treatment in hospital for acute heart failure patients, but not a good predictor after 30 days discharge. From the ROC curve, the cut-off serum potassium levels at the admission was 4.45 meq/L with 64% sensitivity and 75% specificity. Optimum cut-off points potassium ≥ 4.45 mEq/L can predict major cardiovascular events in hospital of acute heart failure patients with good sensitivity and specificity.

Conflict of interest: None declared

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