Clinical Prediction Model for Hypokalemia in Hospitalized Patients with Acute Decompensated Heart Failure Treated with Intravenous Furosemide

Yutthana Rakphaka, Panthita Sornhiran

Division of Nephrology, Department of Internal Medicine, Police General Hospital, Bangkok, Thailand

Abstract

Background: Hospitalized patients with acute heart failure often receive furosemide, which may lead to hypokalemia. Factors such as diuretic dose and concomitant use of multiple diuretics are associated with this risk. This study aimed to develop a clinical prediction model for hypokalemia to help prevent its occurrence and related complications.

Methods: This is a retrospective clinical study of hospitalized patients with acute decompensated heart failure (ADHF). Using multivariable logistic regression, we derived a prediction score by assigning weights to the predictor coefficients. The score was then internally validated to assess its reliability.

Results: Among 510 hospitalized patients with ADHF receiving furosemide, 143 (28%) developed hypokalemia. Furosemide doses >1.5 mg/kg/day were strongly associated with hypokalemia (adjusted OR 4.81, 95% CI 2.56–9.04, p <0.001). Five predictors were identified: baseline serum potassium <4 mmol/L, serum albumin >3.5 g/dL, low serum magnesium, furosemide dose >1.5 mg/kg, and no prior spironolactone use. Higher scores were associated with an increased risk of hypokalemia.

Conclusions: The clinical prediction model provides a practical tool for estimating the risk of hypokalemia. ADHF patients identified as high risk may benefit from preventive strategies and closer monitoring of potassium levels.

Keywords: CHF; volume overload; diuretics; hypomagnesemia; potassium-sparing diuretics

Corresponding author: *Panthita Sornhiran*
Email: *panthita.sornhiran@gmail.com*

Received: 7 September 2025; Revised: 20 October 2025; Accepted: 23 October 2025
https://doi.org/ 10.63555/jnst.2025.282304

แบบจำลองการทำนายทางคลินิกของความเสี่ยงภาวะโพแทสเซียมต่ำในผู้ป่วยภาวะหัวใจล้มเหลวเฉียบพลันที่เข้ารับการรักษาในโรงพยาบาลหลังจากได้รับยาขับปัสสาวะฟูโรซีไมด์

ยุทธนา รักผกา, ปัณฑิตา ศรหิรัญ

หน่วยโรคไต กลุ่มงานอายุรกรรม โรงพยาบาลตำรวจ

บทคัดย่อ

บทนำ: ผู้ป่วยโรคหัวใจล้มเหลวเฉียบพลันที่เข้ารับการรักษาในโรงพยาบาลมักได้รับยาฟูโรเซไมด์ ซึ่งอาจนำไปสู่ภาวะโพแทสเซียมในเลือดต่ำ ปัจจัยเสี่ยงที่เกี่ยวข้อง ได้แก่ ขนาดยาขับปัสสาวะและการใช้ยาขับปัสสาวะหลายชนิดร่วมกัน วัตถุประสงค์ของการศึกษานี้คือเพื่อพัฒนาโมเดลทำนายความเสี่ยงภาวะโพแทสเซียมต่ำทางคลินิก เพื่อช่วยในการป้องกันการเกิดภาวะดังกล่าวและภาวะแทรกซ้อนที่เกี่ยวข้อง

ระเบียบวิธีวิจัย: เป็นการศึกษาย้อนหลังในผู้ป่วยที่เข้ารับการรักษาในโรงพยาบาลด้วยภาวะหัวใจล้มเหลวเฉียบพลัน (Acute Decompensated Heart Failure หรือ ADHF) โดยใช้การวิเคราะห์ถดถอยโลจิสติกพหุคูณ (multivariable logistic regression) เพื่อสร้างคะแนนทำนายความเสี่ยงจากการถ่วงน้ำหนักของตัวแปรทำนาย และทำการตรวจสอบความถูกต้องภายใน (internal validation) เพื่อประเมินความน่าเชื่อถือของโมเดล

ผลการศึกษา: ในกลุ่มผู้ป่วย ADHF จำนวน 510 รายที่ได้รับฟูโรเซไมด์ พบว่ามีผู้ป่วย 143 ราย (28%) ที่เกิดภาวะโพแทสเซียมต่ำ การได้รับฟูโรเซไมด์ในขนาด >1.5 มก./กก./วัน มีความสัมพันธ์อย่างมีนัยสำคัญกับภาวะโพแทสเซียมต่ำ (Adjusted OR 4.81, 95% CI 2.56–9.04, p<0.001) โดยพบปัจจัยทำนาย 5 ประการ ได้แก่ ระดับโพแทสเซียมในซีรั่ม <4 มิลลิโมล/ลิตร., ระดับอัลบูมินในซีรั่ม >3.5 กรัม/ดล., ระดับแมกนีเซียมต่ำ, การได้รับฟูโรเซไมด์ >1.5 มก./กก. และการไม่เคยได้รับสไปโรโนแลคโตนมาก่อน คะแนนที่สูงขึ้นสัมพันธ์กับความเสี่ยงในการเกิดภาวะโพแทสเซียมต่ำที่เพิ่มขึ้น

สรุป: โมเดลทำนายทางคลินิกนี้เป็นเครื่องมือที่มีประโยชน์ในการประเมินความเสี่ยงของภาวะโพแทสเซียมต่ำ ผู้ป่วย ADHF ที่ถูกระบุว่ามีความเสี่ยงสูงอาจได้รับประโยชน์จากการป้องกันและการติดตามระดับโพแทสเซียมอย่างใกล้ชิด

คำสำคัญ: โปแตสเซียมต่ำ; หัวใจวาย; น้ำท่วมปอด; ยาขับฉี่

Introduction

Acute heart failure is a medical emergency that often requires hospitalization. Loop diuretics, such as furosemide, are considered the first-line treatment for this condition. By promoting diuresis, loop diuretics rapidly relieve fluid overload and improve clinical status.[1] However, furosemide can cause various electrolyte disturbances, including hypokalemia and hypomagnesemia.[2] In patients with acute heart failure, hypokalemia may lead to serious consequences such as arrhythmias, muscle weakness, and increased mortality.[3]

Hypokalemia is generally defined as a serum potassium concentration <3.5 mmol/L.[4] The relationship between serum potassium levels and morbidity or mortality

ผู้ประพันธ์บรรณกิจ: *ปัณฑิตา ศรหิรัญ*
อีเมล: *panthita.sornhiran@gmail.com*

รับบทความ: 7 กันยายน 2568; ปรับปรุงแก้ไข: 20 ตุลาคม 2568; รับตีพิมพ์: 23 ตุลาคม 2568

follows a U-shaped curve.[5] According to Ziying Lin et al., hypokalemia occurs in up to 21% of hospitalized patients, and in up to 56% when diuretics are used, depending on type and dose. Risk factors include higher diuretic doses, female sex, and use of multiple diuretics. The use of angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, or angiotensin receptor–neprilysin inhibitors is associated with a decreased risk of hypokalemia among individuals who use diuretics.[6]

A study by Aimbudlop et al. identified additional factors associated with hypokalemia following furosemide administration, including reduced glomerular filtration rate, urine output >2 mL/kg/hour, furosemide dose >1.5 mg/kg, and low serum albumin.[7] To date, there has been no study of a clinical prediction model for hypokalemia following furosemide treatment in acute decompensated heart failure (ADHF). This study aims to address the knowledge gap by identifying key predictors of hypokalemia, developing a risk stratification model, and providing a framework to guide preventive strategies.

Material and methods

Study Population

This retrospective case-control study included hospitalized patients with ADHF who received intravenous furosemide. Data were collected from the medical records of patients admitted to Police General Hospital between 2017 and 2024. Patients with ADHF were identified using International Classification of Diseases (ICD-10) codes. The study was approved by the Ethics Committee of Police General Hospital, which granted a waiver of informed consent.

Eligible patients were ≥18 years old and had received at least 40 mg of intravenous furosemide within 24 hours of admission. Additional inclusion criteria were an estimated glomerular filtration rate (eGFR) of ≥ 30 mL/min/1.73 m² and a baseline serum potassium level between 3.5 – 4.5 mEq/L. Exclusion criteria included hemodynamic instability, concomitant or immediate (within 6 hours) use of oral potassium supplements, use of another diuretic with furosemide, and conditions affecting serum potassium levels (e.g., renal tubular acidosis, hyperaldosteronism, thyrotoxicosis, Bartter syndrome, Gitelman syndrome). Patients with conditions that increase serum potassium levels (e.g., hypoaldosteronism, obstructive uropathy, rhabdomyolysis, hemolysis, tumor lysis syndrome) or those undergoing kidney transplantation were also excluded.

Outcomes

The outcome was to develop a clinical prediction model for hypokalemia in hospitalized patients with ADHF after receiving intravenous furosemide and to validate the model internally using the data from the same hospital.

Data collection

Baseline demographic data were collected. Baseline laboratory results were obtained prior to the administration of furosemide. During hospitalization, urine output, furosemide dosage, follow-up laboratory results, and length of stay were recorded.

Development of Clinical Prediction Model

The dataset was divided into two parts. Predictors of hypokalemia (defined as serum potassium <3.5 mmol/L) were initially identified to construct the model. The model's predictive performance was tested after furosemide administration.

Sample size calculation

The sample size was calculated based on the study by Aimbudlop K et al.[7], which reported a 28.86% incidence of hypokalemia in patients with acute heart failure treated with furosemide. Using a one-proportion formula, the required sample size was estimated at 495 patients.[8]

Statistical Analysis

Continuous variables were summarized as the median with interquartile range (IQR) or as the mean ± standard deviation (SD), while categorical variables were presented as frequencies. Group comparisons were performed using the Chi-square test or Fisher's exact test for categorical variables, and the Wilcoxon rank-sum test or independent t-test for continuous variables.

Univariable and multivariable logistic regression analyses were conducted to identify predictors of hypokalemia. Multicollinearity was checked using

variance inflation factors. Variables with p <0.20 in univariable analysis were entered into the multivariable model using forward stepwise selection. Only variables with p <0.05 were retained. A p-value <0.05 was considered statistically significant.

The clinical prediction model was developed by calculating correlation coefficients and likelihood ratios using a multivariable logistic regression model. Model performance was assessed with the Hosmer-Lemeshow goodness-of-fit test, Bayesian Information Criterion (BIC), Akaike Information Criterion (AIC), observed-to-expected (O/E) ratio, and the area under the receiver operating characteristic curve (AUC). Internal validation was performed. All statistical analyses were conducted using SPSS version 26.

Results

Seven hundred patients with ADHF who were hospitalized were identified. A total of 190 patients were excluded, resulting in 510 patients included in the final analysis. Among these patients, 143 patients had hypokalemia, and 367 patients were normokalemic. The study flow diagram is depicted in **Figure 1**.

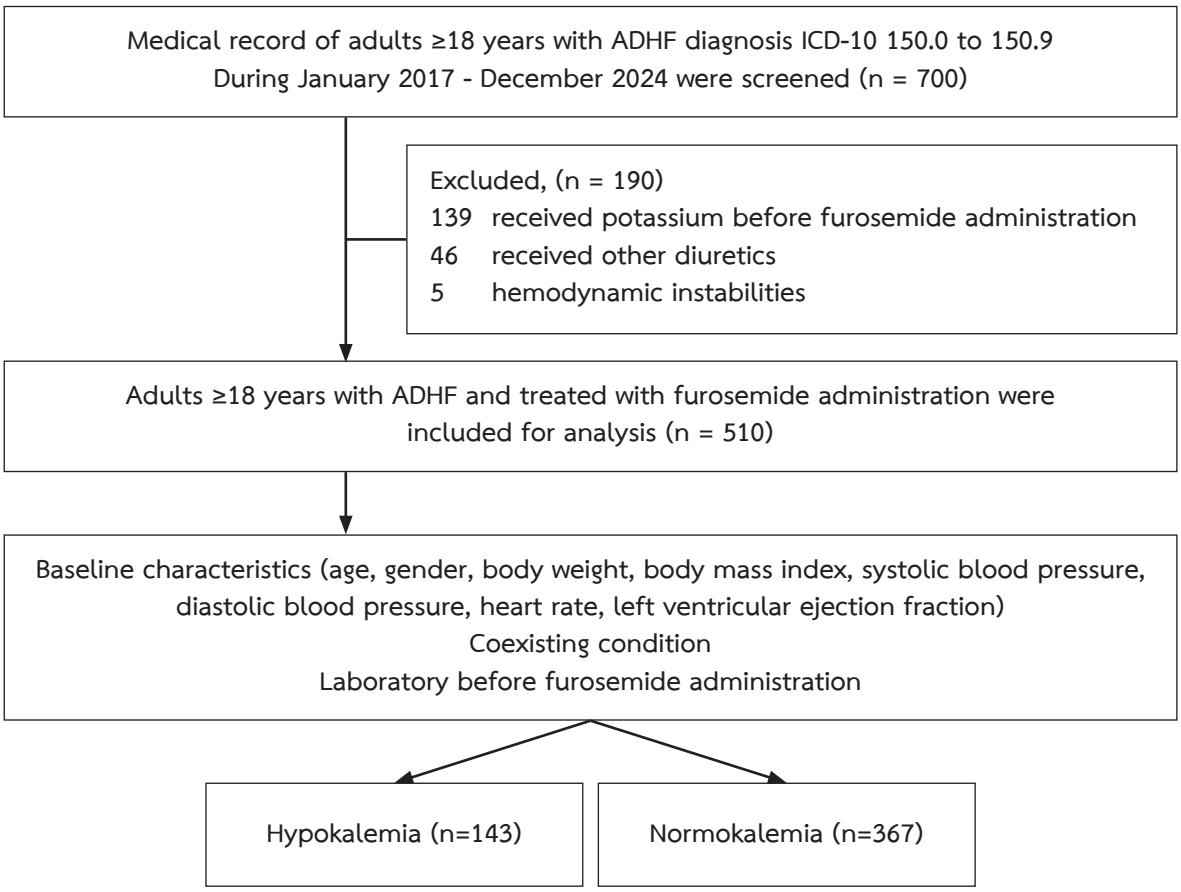

Figure 1 Study flow diagram of patients

Baseline demographic and laboratory data of all patients, categorized by normokalemia/hypokalemia status, are shown in **Table 1**. Patients in the hypokalemia group showed a lower percentage of males, as well as lower body weight, body mass index, baseline serum potassium, and magnesium levels. Additionally, the hypokalemic group showed higher baseline serum albumin levels and received higher doses of spironolactone. The remaining demographic and laboratory data were equivalent between the hypokalemic and normokalemic groups.

Table 1 Baseline demographic and laboratory data of all patients

Parameters	All patients N = 510	Normokalemia N = 367	Hypokalemia N = 143	P-value
Age, years	59.8±16.0	59.4±15.8	61.0±16.6	0.320
Male sex, n (%)	274 (53.7)	216 (58.9)	58 (40.6)	<0.001
Body weight, kg	68.0±16.6	69.9±16.3	63.2±16.5	<0.001
Body mass index, kg/m^2	25.4±4.7	25.7±4.6	24.5±4.8	0.010
Systolic BP, mmHg	142.2±24.2	142.8±24.5	140.6±23.4	0.362
Diastolic BP, mmHg	74.8±16.5	75.3±17.0	73.7±15.2	0.341
Heart rate, beats/minute	81.6±18.5	82.1±19.1	80.5±17.1	0.396
Left ventricular EF, %	51.6±15.8	51.8±15.7	51.3±16.2	0.758
Comorbidities (n/%)				
Hypertension	274 (53.7)	199 (54.2)	75 (52.4)	0.718
Diabetes mellitus	112 (22.0)	79 (21.5)	33 (23.1)	0.704
Cerebrovascular disease	72 (14.1)	49 (13.4)	23 (16.1)	0.426
Heart failure with reduced EF	175 (34.3)	117 (31.9)	58 (40.6)	0.064
Coronary artery disease	184 (36.1)	132 (36.0)	52 (36.4)	0.933
Atrial fibrillation	87 (17.1)	60 (16.3)	27 (18.9)	0.495
Chronic kidney disease stage 3	218 (42.7)	156 (42.5)	62 (43.4)	0.862
Peripheral arterial disease	42 (8.2)	33 (9.0)	9 (6.3)	0.319
Medications (n/%)				
Oral Furosemide	205 (40.2)	141 (38.4)	64 (44.8)	0.190
Oral furosemide dose equivalent (mg/24 hours)	40.0 (20.0, 40.0)	40.0 (20.0, 40.0)	40.0 20.0, 70.0)	1.000
Spironolactone	85 (16.7)	67 (18.3)	18 (12.6)	0.123
Spironolactone dose equivalent (mg/24 hours)	12.5 (12.5, 25.0)	25.0 (12.5, 25.0)	12.5 (12.5, 12.5)	<0.001
ACEI/ARB/ARNI	219 (42.9)	158 (43.1)	61 (42.7)	0.936
Digoxin	22 (4.3)	15 (4.1)	7 (4.9)	0.687
Beta blocker	217 (42.5)	155 (42.2)	62 (43.4)	0.818
Insulin	30 (5.9)	24 (6.5)	6 (4.2)	0.312
Beta-agonist	20 (3.9)	15 (4.1)	5 (3.5)	0.758
SGLT2 inhibitor	39 (7.6)	27 (7.4)	12 (8.4)	0.693
Thiazides	2 (0.4)	1 (0.3)	1 (0.7)	0.483

Table 1 Baseline demographic and laboratory data of all patients (continued)

Parameters	All patients N = 510	Normokalemia N = 367	Hypokalemia N = 143	P-value
Laboratory data				
Creatinine, mg/dL	1.2±0.3	1.2±0.3	1.2±0.3	0.487
eGFR, mL/min/1.73m^2	62.9±20.8	62.8±20.6	63.2±21.4	0.844
Sodium, mmol/L	135.0±6.0	135.0±6.3	135.1±5.0	0.963
Potassium, mmol/L	3.9±0.3	3.9±0.3	3.8±0.2	<0.001
Potassium ≤4 mmol/L, n (%)	350 (68.6)	237 (67.6)	113 (79.0)	0.002
Bicarbonate, mmol/L	22.9±3.8	23.1±3.7	22.3±3.8	0.044
Magnesium, mg/dL	1.9±0.3	2.0±0.3	1.7±0.3	<0.001
Hypomagnesemia*, n (%)	58 (11.4)	18 (4.9)	40 (27.2)	<0.001
Calcium, mg/dL	8.9±0.6	8.9±0.6	8.8±0.6	0.551
Phosphate, mg/dL	3.3±0.9	3.3±0.9	3.3±0.9	0.317
Albumin, g/dL	3.4±0.5	3.4±0.5	3.5±0.4	0.002
Hemoglobin, g/dL	11.8±1.8	11.8±1.7	11.7±2.0	0.641

BP, blood pressure; EF, ejection fraction; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor neprilysin inhibitor; SGLT2, type 2 sodium-glucose transporter; eGFR, estimated glomerular filtration rate. *serum magnesium <1.6 mg/dL

Table 2 illustrates biochemical parameters after the treatment with intravenous furosemide. The hypokalemia group showed lower serum bicarbonate levels, a greater reduction in systolic blood pressure, a higher furosemide dose, and urine output, as well as a longer hospital stay.

Table 2 Biochemical parameters after the treatment with intravenous furosemide

Parameters	Total N = 510	Normokalemia N = 367	Hypokalemia N = 143	P-value
Laboratory data				
Creatinine, mg/dL	1.2±0.3	1.2±0.3	1.2±0.3	0.766
eGFR, mL/min/1.73m^2	61.9±19.7	61.7±19.5	62.5±20.2	0.688
Sodium, mmol/L	136.6±5.0	136.7±5.3	136.3±4.2	0.349
Potassium, mmol/L	3.6±0.3	3.8±0.2	3.2±0.2	<0.001
Bicarbonate, mmol/L	24.3±3.8	24.6±3.8	23.8±3.7	0.044
Decrease in serum potassium >15% from baseline, n (%)	103 (20.2)	20 (5.5)	83 (58.0)	<0.001
Decrease in systolic BP from baseline, mmHg	12.4±8.3	11.8±7.6	13.9±9.7	0.010

Table 2 Biochemical parameters after the treatment with intravenous furosemide (continued)

Parameters	Total N = 510	Normokalemia N = 367	Hypokalemia N = 143	P-value
Furosemide dose				
Total dose, mg/day	80.0 (40.0, 120.0)	80.0 (40.0, 80.0)	120.0 (80.0, 160.0)	<0.001
Dose/kg of body weight/day, mg/kg/day	1.20 (0.70, 1.70)	1.00 (0.67, 1.40)	1.80 (1.30, 2.10)	<0.001
Dose/kg of body weight/day >1.5 mg/kg/day, n (%)	185 (36.3)	84 (22.9)	101 (70.6)	<0.001
Urine output				
24-hour urine output, ml	2630 (2170, 3200)	2480 (2110, 2850)	3450 (2810, 3800)	<0.001
Urine output >2 mL/kg of body weight/hour, n (%)	168 (32.9)	74 (20.2)	94 (65.7)	<0.001
Length of stay, days	9.0 (6.0, 14.0)	8.0 (6.0, 13.0)	10.0 (7.0, 15.0)	0.013

BP, blood pressure; eGFR, estimated glomerular filtration rate

The predictive risk factors for hypokalemia as determined by univariable and multivariable logistic regression are presented in **Table 3**. Variables with p-value <0.2 from Tables 1 and 2 were included in the multivariate model. Serum potassium ≤4 mmol/L, serum albumin >3.5 g/dL, no prior spironolactone use, hypomagnesemia, and intravenous furosemide dose >1.5 mg/kg/day were independent predictors of hypokalemia.

Table 3 Logistic regression analysis of predictive factors for hypokalemia

Factors	Univariable analysis			Multivariable analysis		
	OR	95% CI	*P*	OR	95% CI	*P*
Baseline serum potassium ≤4 mmol/l	2.24	1.27 – 3.93	0.005	2.26	1.15 – 4.45	0.018
Baseline serum albumin >3.5 g/dL	1.95	1.22 – 3.11	0.005	2.29	1.27 – 4.11	0.006
No prior use of spironolactone	1.59	0.80 – 3.16	0.183	2.79	1.20 – 6.48	0.017
Baseline hypomagnesemia	7.11	4.25 – 11.89	<0.001	5.44	3.01 – 9.81	<0.001
Furosemide dose >1.5 mg/kg/day	8.21	4.86 – 13.86	<0.001	7.79	4.27 – 14.21	<0.001
BMI	0.96	0.90 – 1.01	0.108			
HFrEF	1.42	0.88 – 2.28	0.152			
Male	0.51	0.25 – 1.05	0.068			

OR, odds ratio; 95%CI, 95% confidence interval.

During the development phase of the clinical prediction model, we employed a multivariable logistic regression model as outlined in **Table 4**. The linear equation was represented as log-odds as shown in **Figure 2**.

Table 4 Multivariate logistic regression analysis in the development phase

Predictive risk factors	Coefficients	OR (95% CI)	P-value
Intercept	-4.37	0.01 (0.004, 0.04)	<0.001
Serum potassium ≤4 mmol/l	0.82	2.26 (1.15, 4.45)	0.018
Serum albumin >3.5 g/dl	1.69	2.29 (1.27, 4.11)	0.006
No prior use of spironolactone	2.05	2.79 (1.20, 6.48)	0.017
Hypomagnesemia	1.03	5.44 (3.01, 9.81)	<0.001
Furosemide dose >1.5 mg/kg/day	0.83	7.79 (4.27, 14.21)	<0.001

OR, odds ratio; 95%CI, 95% confidence interval

$$ln\left[\frac{P}{1-P}\right] = -4.37 + 0.82 \times \text{Potassium} + 1.69 \times \text{Hypomagnesemia} + 2.05 \times \text{Furosemide dose} + 1.03 \times \text{Albumin} + 0.83 \times \text{Spironolactone}$$

Figure 2 The Coefficients Model

Potassium, serum potassium ≤4 mmol/; Furosemide dose, furosemide dose >1.5 mg/kg/day; Albumin, Albumin >3.5 g/dL; spironolactone, No prior use of spironolactone

The odds ratio score for individual predictive factors is as follows: serum potassium ≤4 mmol/l = 2 points, serum albumin >3.5 g/dL = 2 points, no prior use of spironolactone = 3 points, hypomagnesemia = 5 points, intravenous furosemide dosage >1.5 mg/kg/day = 8 points, and patients with no risk factors as defined individually = 1 point for each factor. The cut-off scores were established using the likelihood ratio, sensitivity, specificity, positive predictive value, and negative predictive value as shown in Table 5. The score ranged from 5 to 20, with higher scores indicating a greater likelihood of hypokalemia. The score is divided into three categories: low probability of hypokalemia (5 – 9), intermediate probability (10 – 14), and high probability (15 – 20).

The Hosmer-Lemeshow test was conducted to evaluate the goodness of fit, yielding a p-value of 0.287 for the model in the development phase. The areas under the curve of the clinical prediction model during the development and internal validation phases were 0.84 and 0.79, respectively **(Table 6)**. To assess the performance of the prediction model, a receiver operating characteristic (ROC) curve was generated **(Figure 3)**.

Table 5 The cut-off scores in the development phase

Cut-off score	LR+	Sensitivity	Specificity	PPV	NPV
≥ 6	1.0	100.0	2.4	29.4	100.0
≥ 10	2.3	83.2	63.1	47.7	90.2
≥ 15	4.7	67.3	85.5	65.4	86.6
≥ 17	11.0	48.5	95.6	81.7	82.1

LR, likelihood ratio; PPV, positive predictive value; NPV, negative predictive value

Table 6 Performance of risk prediction model in development and internal validation

Models	AUC (95% CI)	HL-GOF (df) P-value	O/E Median (IQR)	BIC/AIC
Development	0.842 (0.795, 0.889)	5.00 (3) 0.287	1.01 (0.94, 1.13)	328.73/305.58
Internal validation	0.793 (0.705, 0.880)	2.93 (3) 0.403	1.01 (0.98, 1.08)	151.60/145.49

AUC, area under the curve; 95%CI, 95% confidence interval; HL-GOF, Hosmer and Lemeshow goodness of fit; BIC, Schwarz's Bayesian Information Criterion; AIC, Akaike Information Criteria

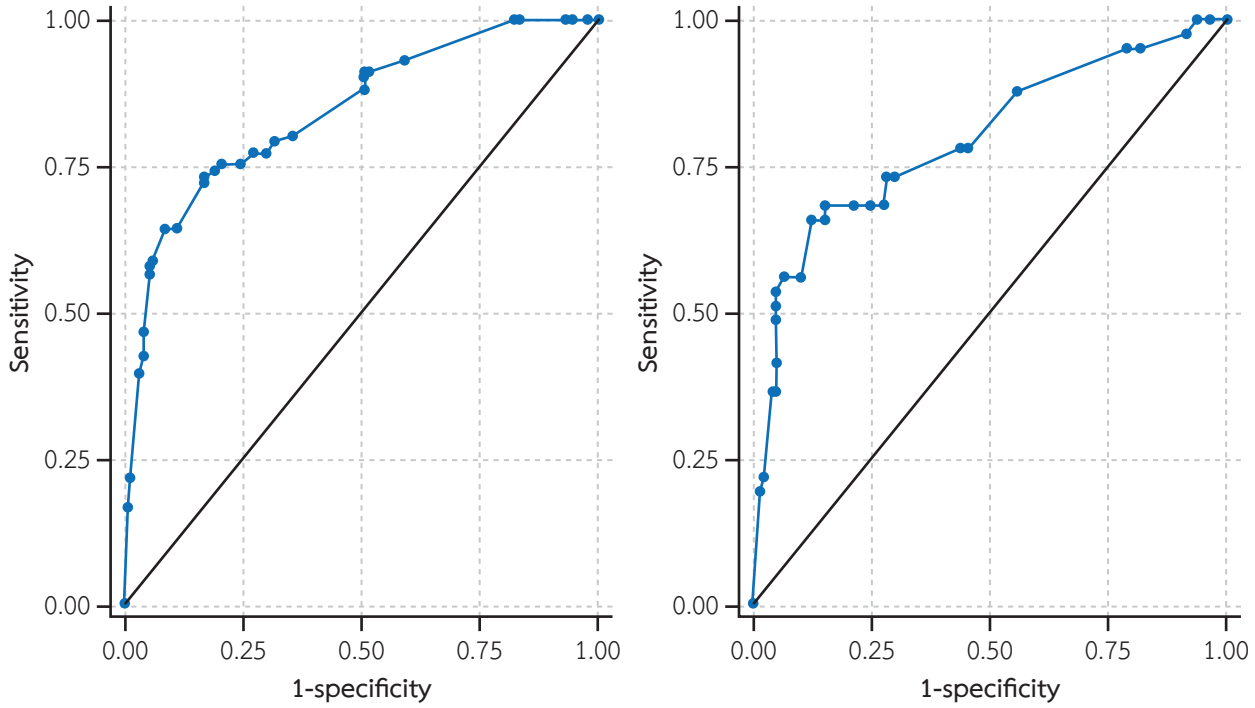

Figure 3 Performance Assessment Using ROC Curve in Development and Validation Phases
ROC, Receiver Operating Characteristic curve

Discussion

The present study developed a clinical prediction score to evaluate the risk of hypokalemia in hospitalized patients with ADHF receiving intravenous furosemide treatment. The key predictors included serum potassium ≤4 mmol/L, serum albumin >3.5 g/dL, serum magnesium <1.6 mg/dL, no prior use of spironolactone, and furosemide doses exceeding 1.5 mg/kg/day. A scoring system was developed based on these predictors in order to help identify patients at an increased risk of developing hypokalemia.

The present study revealed that an intravenous furosemide dose >1.5 mg/kg/day was significantly associated with hypokalemic incidents. According to findings in the retrospective study in outpatient stable heart failure patients by Kapelios CJ et al., patients who received a higher dose of furosemide (>80 mg/day) were more likely to develop hypokalemia during the follow-up compared to those who received a lower dose (≤80 mg/day) (43.1% vs 6.5%, p<0.001).[9] Furthermore, the hypokalemia group showed a total urine output over 24 hours following furosemide administration that was significantly higher than that of the normokalemia group (3,450 ml vs 2,480 ml, p<0.001).

Hypomagnesemia increases renal potassium excretion, thereby worsening hypokalemia.[10] Magnesium typically inhibits Renal Outer Medullary Potassium (ROMK) channels in the distal nephron; when magnesium levels are deficient, this inhibition is removed, resulting in increased potassium excretion in the urine. Consequently, hypokalemia associated with hypomagnesemia often proves resistant to potassium supplementation alone, necessitating magnesium correction to restore normal potassium levels.[11]

In the present study, a serum albumin >3.5 g/dL was associated with an increased risk of hypokalemia. Furosemide is highly protein-bound, particularly to albumin; therefore, with increased availability of albumin, the transport of furosemide to the thick ascending limb of the loop of Henle is increased, thereby enhancing its natriuretic and kaliuretic effects.[12]

Using data from the EMPHASIS-HF trial, Vardeny et al. investigated whether spironolactone could reduce the incidence of hypokalemia in heart failure patients who were taking loop diuretics. The analysis included 2,737 patients who had heart failure with reduced ejection fraction. Patients who received spironolactone showed a significantly lower incidence of hypokalemia (serum potassium level <3.5 mmol/L) compared to the placebo group (7.2% vs. 18.9%, P <0.001).This results in a relative risk reduction of approximately 62%.[13] The protective effect of spironolactone on hypokalemia was most pronounced among patients who received loop diuretics.[14] The strategic inclusion of spironolactone in the pharmacologic management of heart failure, particularly for patients receiving high-dose loop diuretics, is supported by these findings.

A previous study by Kieneker LM et al. investigating the risk of hypokalemia in ADHF patients receiving loop diuretics revealed that patients with a baseline serum potassium between 3.5 - 3.9 mmol/L were more likely to develop hypokalemia than those with serum potassium between 4.0 - 4.4 mmol/L, emphasizing the importance of monitoring serum electrolytes during the treatment of ADHF with diuretics. This may be essential for the prevention of complications, including arrhythmias, muscle paralysis, and progressive heart failure.[15] The clinical relevance of maintaining optimal potassium levels to prevent adverse outcomes associated with hypokalemia is further shown by the study's focus on a specific and high-risk population.[16]

The strength of this study lies in the development of the first clinical prediction model for hypokalemic risk in hospitalized patients with ADHF following furosemide administration. The limitations include its retrospective design and single-center focus, as well as the lack of external validation. Potential confounders, such as dietary potassium intake, medication adherence, and genetic factors, have not been taken into account, which could impact the risk of hypokalemia. The study examined immediate post-treatment hypokalemia; however, it did not assess long-term clinical outcomes, including rehospitalization and mortality.

Conclusions

The clinical prediction model provides a practical tool for estimating the risk of hypokalemia in hospitalized ADHF patients. Utilizing this scoring system has the potential to reduce adverse events related to hypokalemia. Future studies are needed to validate the prediction model across various populations and to examine the effects of risk-stratification-based interventions on patient outcomes.

References

1. Joseph SM, Cedars AM, Ewald GA, Geltman EM, Mann DL. Acute decompensated heart failure: contemporary medical management. Tex Heart Inst J. 2009;36(6):510-20.
2. Thu Kyaw M, Maung ZM. Hypokalemia-Induced Arrhythmia: A Case Series and Literature Review. Cureus. 2022;14(3):e22940. doi: 10.7759/cureus.22940
3. Krogager ML, Søgaard P, Torp-Pedersen C, Bøggild H, Lee CJ, Bonde A, et al. Impact of plasma potassium normalization on short-term mortality in patients with hypertension and hypokalemia or low normal potassium. BMC Cardiovasc Disord. 2020;20(1):386. doi: 10.1186/s12872-020-01654-3
4. Kim MJ, Valerio C, Knobloch GK. Potassium Disorders: Hypokalemia and Hyperkalemia. Am Fam Physician. 2023;107(1):59-70.
5. Brueske B, Sidhu MS, Schulman-Marcus J, Kashani KB, Barsness GW, Jentzer JC. Hyperkalemia Is Associated With Increased Mortality Among Unselected Cardiac Intensive Care Unit Patients. J Am Heart Assoc. 2019;8(7):e011814. doi: 10.1161/jaha.118.011814
6. Lin Z, Wong LYF, Cheung BMY. Diuretic-induced hypokalaemia: an updated review. Postgrad Med J. 2022;98(1160):477-82. doi: 10.1136/postgradmedj-2020-139701
7. Aimbudlop K, Saengpanit D. Factors Associated with Hypokalemia after Furosemide Treatment in Hospitalized Patients with Acute Decompensated Heart Failure. J Nephrol Soc Thail. 2024;30(1):57-68.
8. Metcalfe C. Biostatistics: A Foundation for Analysis in the Health Sciences. 7th edn. Wayne W. Daniel, Wiley, 1999. No. of. pages: xiv+755+appendices. ISBN 0-471-16386-4. Statistics in Medicine - STAT MED. 2001;20:324-6. doi: 10.1002/1097-0258(20010130)20:2<324::aid-sim635>3.0.co;2-o
9. Kapelios CJ, Kaldara E, Ntalianis A, Sousonis V, Repasos E, Sfakianaki T, et al. High furosemide dose has detrimental effects on survival of patients with stable heart failure. Hellenic J Cardiol. 2015;56(2):154-9.
10. Weiner ID, Wingo CS. Hypokalemia--consequences, causes, and correction. J Am Soc Nephrol. 1997;8(7):1179-88. doi: 10.1681/asn.v871179
11. Huang CL, Kuo E. Mechanism of hypokalemia in magnesium deficiency. J Am Soc Nephrol. 2007;18(10):2649-52. doi: 10.1681/asn.2007070792
12. Brater DC. Diuretic therapy. N Engl J Med. 1998;339(6):387-95. doi: 10.1056/nejm199808063390607
13. Vardeny O, Claggett B, Anand I, Rossignol P, Desai AS, Zannad F, et al. Incidence, predictors, and outcomes related to hypo- and hyperkalemia in patients with severe heart failure treated with a mineralocorticoid receptor antagonist. Circ Heart Fail. 2014;7(4):573-9. doi: 10.1161/circheartfailure.114.001104
14. Epstein M, Calhoun DA. Aldosterone blockers (mineralocorticoid receptor antagonism) and potassium-sparing diuretics. J Clin Hypertens (Greenwich). 2011;13(9):644-8. doi: 10.1111/j.1751-7176.2011.00511.x
15. Kieneker LM, Eisenga MF, Joosten MM, de Boer RA, Gansevoort RT, Kootstra-Ros JE, et al. Plasma potassium, diuretic use and risk of developing chronic kidney disease in a predominantly White population. PLoS One. 2017;12(3):e0174686. doi: 10.1371/journal.pone.0174686
16. Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE, Jr., Colvin MM, et al. 2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. Circulation. 2017;136(6):e137-e61. doi: 10.1161/cir.0000000000000509