

Artificial Intelligence-Enabled Electrocardiography for Monitoring Serum Potassium Dynamics in Patients With Severe Hypokalemia

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Rationale & Objective: Severe hypokalemia requires prompt management and close surveillance. Although artificial intelligence-enabled electrocardiography (AI-ECG) rapidly detects severe hypokalemia, its application for monitoring serum potassium (K^+) dynamics during treatment remains unexplored. This study assessed AI-ECG performance in monitoring K^+ changes during supplementation.

Study Design: Multicenter retrospective cohort study.

Setting & Participants: 191 adults with severe hypokalemia (laboratory-measured [$\text{lab-}K^+$] ≤ 2.5 mmol/L; matched ECG- K^+ < 3.5 mmol/L) and ≥ 1 follow-up paired measurement within 24 hours of K^+ supplementation at 3 teaching hospitals between September 2019 and August 2024.

Exposure: Laboratory-measured K^+ ($\text{lab-}K^+$) and K^+ estimated by ECG (ECG- K^+) overall and stratified by the etiology of hypokalemia (acute K^+ shift vs chronic K^+ deficit).

Outcome: Primary: agreement between paired ECG- K^+ and $\text{lab-}K^+$. Secondary: diagnostic accuracy and K^+ trajectories.

Analytical Approach: Linear mixed-effects models with patient-level random intercepts; repeated-measures correlation (rmcorr) and Bland-Altman plots; patient-level clustered bootstrapped receiver operating characteristic analysis for diagnostic accuracy.

Results: Of 191 patients, 156 (81.7%) had chronic K^+ deficits (most commonly gastrointestinal

disorders [$n = 47$] or diuretic use [$n = 35$]), and 35 (18.3%) had acute K^+ shifts (most commonly thyrotoxic periodic paralysis [$n = 25$]). The chronic K^+ deficits group had more comorbidities and use of medications affecting K^+ . ECG- K^+ correlated strongly with $\text{lab-}K^+$ (rmcorr 0.847 [95% CI, 0.81-0.88], $P < 0.001$). The relationship was modified by hypokalemia etiology (interaction $P < 0.0001$) with a lower correlation in patients with chronic K^+ deficits. The diagnostic accuracy of ECG- K^+ with $\text{lab-}K^+ < 3.5$ mmol/L was reflected by an area under the curve of 0.920 (95% CI, 0.863-0.961). It was higher in patients with an acute K^+ shift. ECG- K^+ preceded $\text{lab-}K^+$ results by a mean of 52.5 minutes. Patients with an acute K^+ shift corrected approximately 3-fold faster than those with a chronic K^+ deficit (0.121 vs 0.039 mmol/L/h). Rebound hyperkalemia was detected by ECG- K^+ in 2 patients before laboratory confirmation.

Limitations: Retrospective design, treatment-protocol heterogeneity, limited inpatient medication granularity, and potential selection bias.

Conclusions: AI-ECG enables real-time, within-patient monitoring of serum K^+ dynamics during treatment for severe hypokalemia, with superior performance in the setting of acute hypokalemia due to K^+ shift. As a noninvasive adjunct, AI-ECG may shorten the time to detect changes in K^+ and reduce the need for $\text{lab-}K^+$ measurements rather than relying exclusively on $\text{lab-}K^+$. Confirmatory studies are warranted.

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Hypokalemia, the most common electrolyte imbalance in hospitalized patients, is associated with increased cardiovascular morbidity and mortality.^{1,2} It has been reported that approximately 10% to 15% of hospitalized patients or patients at the emergency department (ED) had hypokalemia (serum potassium [K^+] < 3.5 mmol/L).³ The prevalence is particularly high among patients with gastrointestinal disorders and those receiving diuretic therapy.^{4,5} Because hypokalemia can be acute due to an increased shift of K^+ into cells, or chronic, related to K^+ deficits, the principal treatment is low-dose K^+ supplementation in acute K^+ shifts and a higher dosage of K^+ in chronic K^+ deficits.⁶⁻¹⁰ Severe hypokalemia (serum $K^+ \leq 2.5$ mmol/L) is a life-threatening condition associated

with potentially fatal arrhythmias and cardiac death, so special attention is warranted for prompt recognition with swift therapy and careful monitoring during treatment.^{5,6,8,11-13}

In clinical practice, the diagnosis of hypokalemia relies primarily on laboratory measurement. Because cardiac tissue is very sensitive to hypokalemia, electrocardiography (ECG) as a prompt, noninvasive bedside tool may detect the electrical changes associated with hypokalemia. The main ECG changes related to hypokalemia include decreased T wave amplitude, ST-segment depression, T wave inversion, prolonged PR interval, and increased corrected QT interval (QTc).¹⁴⁻¹⁶ However, even experienced physicians may not consistently recognize severe hypokalemia-related ECG changes.^{14,15} Recent advances in artificial intelligence (AI),

PLAIN-LANGUAGE SUMMARY

Severe hypokalemia, or very low blood potassium, is common in hospitalized patients and can cause dangerous heart rhythms. In clinical practice, potassium levels are often monitored with blood tests whose results are not immediately available. This study assessed whether an artificial intelligence (AI) tool that estimates blood potassium levels from a standard electrocardiogram (ECG) tracing can reduce the need for laboratory testing of blood for potassium levels. Patients with hypokalemia at 3 hospitals were studied. AI-based estimates of blood potassium were obtained very close in time to when blood was drawn for laboratory measurements of potassium. The AI-based estimates were available almost an hour earlier than laboratory tests, and both values were very similar. The similarity was greater when the hypokalemia was caused by a sudden shift into cells rather than chronic potassium loss from the body. AI-based estimates of potassium potentially offer a faster, noninvasive way to track potassium changes for patients over time, to guide potassium replacement, to reduce the need for repeated blood draws, and to detect dangerously high levels of potassium earlier.

particularly deep learning models (DLMs), have transformed the landscape of ECG analysis.¹⁷⁻²² Using large ECG-annotated datasets, we first successfully applied DLM to develop ECG-based quantitative detection of hypokalemia in the ED.^{20,23} Our AI-ECG system using 12-lead ECG analysis achieved an area under the curve (AUC) of 0.95 with a sensitivity of 93.3% for severe hypokalemia, significantly outperforming human experts.^{23,24}

In severe hypokalemia, frequent monitoring of serum K^+ levels is warranted to avoid cardiac arrhythmia and evaluate treatment effect.^{1,25} Although the artificial intelligence-enabled electrocardiography (AI-ECG) system offers real-time prediction of serum K^+ levels, its clinical application for monitoring serum K^+ changes during severe hypokalemia treatment has yet to be evaluated. In this multicenter retrospective cohort study with repeated measures, we assessed the agreement between AI-ECG predicted potassium (ECG- K^+) and laboratory-measured potassium (lab- K^+) during K^+ supplementation therapy in patients with severe hypokalemia and determined whether hypokalemia etiology (acute K^+ shift vs chronic K^+ deficit) modifies the ECG- K^+ /lab- K^+ relationship.

Methods**Study Design and Population**

This multicenter retrospective observational cohort study with repeated measures was conducted at 3 teaching hospitals in Taiwan (Tri-Service General Hospital, Taipei;

Armed Forces Kaohsiung General Hospital, Kaohsiung; and Armed Forces Taoyuan General Hospital, Taoyuan) between September 2019 and August 2024. The study protocol was approved by the institutional review boards of all participating centers (TSGHIRB C202505133), and the requirement for informed consent was waived due to the retrospective nature of the study. Patients or members of the public were not involved in the design, conduct, reporting, or dissemination plans of this research.

The study retrospective design relied entirely on de-identified electronic medical records and routinely collected ECG and laboratory data, with no direct patient contact or recruitment during the study. The findings will be communicated to clinical staff at the participating institutions through internal grand rounds and incorporated into institutional electrolyte-management protocols and clinician training, alongside dissemination through peer-reviewed publication and lay-language summaries for the broader medical community.

The inclusion criteria were (1) adult patients (≥ 18 years) with at least 1 serum K^+ measurement of ≤ 2.5 mmol/L; (2) a 12-lead ECG obtained concurrently with the K^+ blood draw (within 1 hour), with a matched ECG- K^+ measurement of < 3.5 mmol/L at baseline; and (3) at least 1 additional paired ECG- K^+ /lab- K^+ measurement obtained during K^+ supplementation (within 24 hours of the initial pair). The exclusion criteria were (1) absence of follow-up paired ECG- K^+ /lab- K^+ measurements during the correction period; and (2) a poor-quality ECG precluding AI analysis.

Data Collection

We extracted the following data from electronic medical records: demographic information (age, sex assigned at birth), clinical characteristics, relevant laboratory values, details of K^+ supplementation therapy, paired ECG- K^+ and lab- K^+ measurements with corresponding timestamps, underlying etiologies of hypokalemia, and, when available, echocardiographic findings. Based on clinical evaluation, laboratory findings, and established diagnostic criteria, the patients were classified into having either acute K^+ shift hypokalemia or chronic K^+ deficit hypokalemia.²⁶⁻³³

Treatment of Severe Hypokalemia

As suggested by the standard clinical guidelines and our previous studies for severe hypokalemia, K^+ therapy was administered via intravenous and/or oral supplementation at rates of 10-20 mmol/h for acute K^+ shift and ≥ 20 mmol/h for chronic K^+ deficit. The K^+ dosage was also adjusted by physicians based on the clinical scenario, treatment response, and serial monitoring.^{5,6,9,34}

Measurements of Lab- K^+ and ECG- K^+

Lab- K^+ was determined by ISO-certified central laboratories at each participating institution. Blood samples were analyzed using indirect ion-selective electrode technology

with automated analyzers. ECG-K⁺ was computed using the previously validated ECG12Net deep learning model.²³ This model analyzes morphologic variations in standard 12-lead ECGs captured on Philips ECG machines (Model PH080A) through 82 convolutional layers rather than relying on conventional ECG parameters such as intervals and amplitudes. The ECG12Net model was trained on a large dataset of ECGs with paired serum K⁺ measurements and achieves high accuracy for detecting electrolyte abnormalities, with a previously reported AUC of 0.950 for severe hypokalemia.²³

The AI-ECG analysis system visualizes K⁺ levels through a 12-lead ECG format, with each lead contributing a weighted prediction to the final estimated value (Fig S1). The algorithm's output is calibrated within a predefined range of 1.5 to 7.5 mmol/L, based on the parameters established during model training. For analysis purposes, hypokalemia severity during K⁺ therapy was classified as severe (lab-K⁺ ≤ 2.5 mmol/L), moderate (lab-K⁺ 2.6-3.0 mmol/L), and mild (lab-K⁺ 3.1-3.5 mmol/L).

Timing of Paired Measurements

ECG recordings and laboratory blood draws were obtained as part of routine clinical care during the potassium correction process. The first paired ECG-K⁺/lab-K⁺ measurement of every patient was obtained at the time of presentation before the initiation of K⁺ supplementation, and subsequent paired measurements were obtained during the K⁺ correction phase. The frequency of follow-up measurements was not fixed and was determined by clinical necessity, as guided by the treating physician. Two distinct timing concepts are reported separately in the results: the ECG-to-blood-draw gap (near-simultaneous capture during routine care) and the laboratory result turnaround (specimen processing delay until the result became available to clinicians). Each such paired observation is referred to as a time point in the subsequent analyses.

Statistical Analysis

Continuous variables are reported as median and interquartile range or mean ± standard deviation, and categorical variables as number and percentage. To account for within-patient correlation arising from repeated measurements during K⁺ supplementation, a linear mixed-effects model (dependent variable, lab-K⁺; independent variable, ECG-K⁺) with patient-level random intercepts was used as the primary analysis:

$$\text{lab-K}^+_{ij} = \beta_0 + \beta_1 \times \text{ECG-K}^+_{ij} + u_i + \varepsilon_{ij}$$

where $u_i \sim N(0, \sigma^2_u)$ is the random intercept for patient i . Etiology-based interaction was tested by adding an ECG-K⁺ × etiology term to the model and comparing via likelihood ratio test. Repeated-measures correlation (rmcorr) quantified the within-patient correlation, and Bland-

Altman analysis assessed the agreement. Between-group differences in ECG-K⁺/lab-K⁺ correlations were tested using a z test after Fisher's z transformation, reported as a descriptive comparison. As a sensitivity analysis, generalized estimating equations (GEE) were also fitted to confirm robustness of the primary estimates.

The diagnostic accuracy of ECG-K⁺ for hypokalemia was assessed at the standard threshold of lab-K⁺ < 3.5 mmol/L (with the same cutoff applied to ECG-K⁺). Sensitivity, specificity, and the area under the receiver operating characteristic curve (AUC-ROC) were computed overall and within acute and chronic etiology subgroups; AUC 95% confidence intervals were derived by patient-level clustered bootstrap (5,000 resamples) to account for within-patient correlation. Per-stratum detection rates were additionally reported within lab-K⁺ severity strata.

Correction trajectories during K⁺ supplementation were analyzed using a mixed-effects model with time, etiology, and a time × etiology interaction term, also evaluated by likelihood ratio test. Detailed model specifications, equations, and bootstrap procedures are provided in Item S1. A 2-sided P value < 0.05 was considered statistically significant. All analyses were performed using Python 3.11.

Results

Patient Characteristics

As shown in Figure 1, a total of 413 patients visiting the ED had severe hypokalemia (lab-K⁺ ≤ 2.5 mmol/L) with a matched ECG within 1 hour, and 397 of these patients had a concurrent ECG-K⁺ < 3.5 mmol/L. After exclusion of the patients without follow-up ECG-K⁺ measurements, there were 191 patients with severe hypokalemia, comprising 466 paired measurements that fulfilled the inclusion criteria. A majority ($n = 180$) were enrolled from the tertiary medical center. Compared with the 222 contemporaneously screened but excluded patients, the included patients had a similar age, sex, and acute K⁺ shift etiology distribution (Table S1).

The patients' baseline characteristics are shown in Table 1. The median age was 59.5 years (IQR, 42.4-78.9), and they were predominantly men (111 of 191 patients, 58.1%). Chronic K⁺ deficit accounted for 81.7% ($n = 156$) of patients, with gastrointestinal disorders ($n = 47$), diuretics ($n = 35$), and Bartter/Gitelman syndrome ($n = 23$) being the most common causes. In 35 patients (18.3%) with an acute K⁺ shift, thyrotoxic periodic paralysis (TPP) was the most common cause ($n = 25$), followed by sporadic periodic paralysis ($n = 7$) and medication-related causes ($n = 3$). The patients with an acute K⁺ shift were younger (median, 36.3 vs 64.3 years) and predominantly men (94.3% vs 50.0%). The patients with chronic K⁺ deficit had a higher prevalence of diabetes mellitus (37.2% vs 14.3%), hypertension (47.4% vs 17.1%), heart failure (19.9% vs 2.9%), and outpatient K⁺-

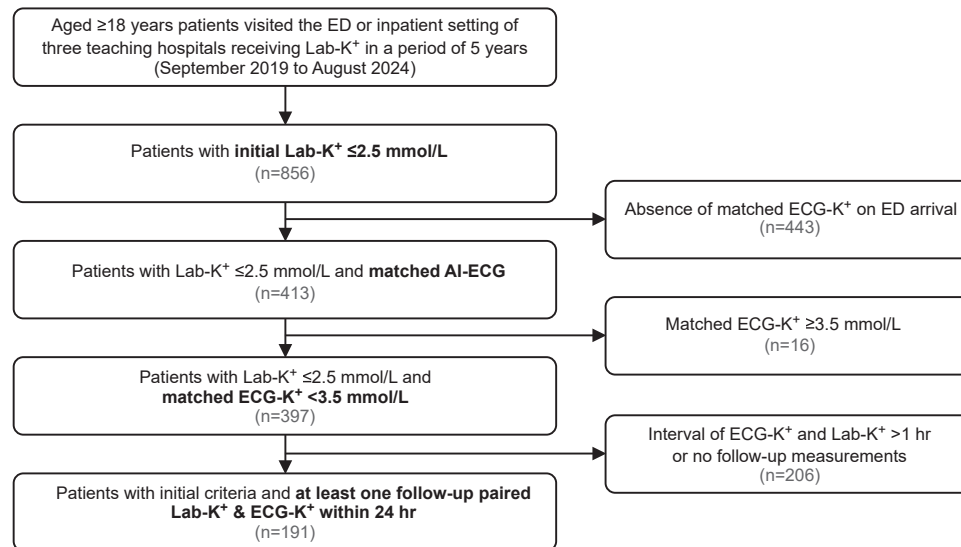


Figure 1. Patient selection flowchart for severe hypokalemia with paired AI-ECG monitoring. Abbreviations: AI-ECG, artificial intelligence-enabled electrocardiography; ECG-K⁺, serum potassium estimated by electrocardiography; ED, emergency department; lab-K⁺, laboratory measured serum potassium.

affecting medication use (50.0% vs 34.3%). Within the K⁺-affecting composite, chronic K⁺-wasting agents predominated in the chronic group, while preadmission insulin was more frequent in the acute group (Table S2). Patients with an acute K⁺ shift presented with slightly lower lab-K⁺ levels compared with the chronic group (2.11 ± 0.39 vs 2.22 ± 0.28 mmol/L).

In total, 466 paired lab-K⁺ and ECG-K⁺ measurements were obtained in 191 patients, with 1 or more follow-up pairs within 24 hours of K⁺ supplementation: 74.3% (142 of 191) contributed 1 follow-up paired measurement, 15.2% (29 of 191) had 2 pairs, and 10.5% (20 of 191) had 3 or more pairs. Each patient contributed a median of 2 paired measurements (IQR, 2-3), with within-patient clustering (intraclass correlation coefficient for lab-K⁺ = 0.323).

Correlation, Agreement, and Diagnostic Accuracy

Across these paired measurements, ECG-K⁺ correlated strongly with lab-K⁺ on repeated-measures analysis (rmcorr, 0.847 [95% CI, 0.81-0.88], $P < 0.001$) (Fig 2A), and Bland-Altman analysis demonstrated good agreement, with the large majority of measurements within the limits of agreement (Fig 2B). Discrepant cases (>0.5 mmol/L; 138 [29.6%]) were characterized by older age (median, 63.1 vs 55.9 years; $P = 0.011$) (Table S3).

The mixed-effects modeling demonstrated etiology-dependent agreement: ECG-K⁺ tracked lab-K⁺ near 1:1 in the acute group but with attenuated slope in the chronic group, with a highly significant ECG-K⁺ × etiology interaction term (likelihood ratio $\chi^2 = 90.0$, degrees of freedom [df] = 1, $P < 0.0001$), and an overall etiology contribution to model fit by joint test ($\chi^2 = 95.4$, df = 2, $P < 0.0001$)

(Table 2). A Fisher z test of between-group correlation differences provided a concordant descriptive comparison ($z = 5.83$, $P < 0.0001$). GEE under alternative working correlation structures was concordant (Table S4), and the bootstrap distribution of the regression estimates supported coefficient stability (Fig S2).

The detection rates of any hypokalemia at this threshold were 97.3% (285 of 293), 91.6% (87 of 95), and 72.5% (29 of 40) for laboratory-defined severe (≤ 2.5 mmol/L), moderate (2.6-3.0 mmol/L), and mild (3.1-3.5 mmol/L) hypokalemia, respectively. ECG-K⁺ retained strong rank-order discrimination at this threshold (AUC, 0.920 [95% CI, 0.863-0.961]), with higher accuracy in patients with an acute K⁺ shift (AUC, 0.952 [95% CI, 0.900-0.993]) than in those with chronic K⁺ deficit (AUC, 0.870 [95% CI, 0.741-0.959]) (Table 3). The ROC curves are provided in Figure S3. Two patients developed rebound hyperkalemia (lab-K⁺ > 5.0 mmol/L) and were correctly flagged by ECG-K⁺ (>5.0 mmol/L).

Timing, Correction Trajectories, and Rebound Hyperkalemia

The ECG recordings and blood draws were near-simultaneous (mean difference, 5.2 ± 23.9 minutes), and ECG-K⁺ results were available a mean of 52.5 ± 29.3 minutes before the laboratory K⁺ reports. Monitoring intensity was highest during early treatment (Fig 3), with measurements concentrated in the first 8 hours. The correction dynamics differed markedly between the etiology groups: patients with an acute K⁺ shift corrected approximately 3-fold faster within the first 4 hours compared with those with a chronic deficit (0.121 vs 0.039 mmol/L/h) (Fig 4), consistent with the rapid

Table 1. Baseline Characteristics by Hypokalemia Etiology

	Overall (n = 191)	Acute K ⁺ Shift (n = 35)	Chronic K ⁺ Deficit (n = 156)
Age, y	59.5 [42.4-78.9]	36.3 [27.5-49.3]	64.3 [48.2-81.1]
Male	111 (58.1%)	33 (94.3%)	78 (50.0%)
Comorbidities			
Diabetes mellitus	63 (33.0%)	5 (14.3%)	58 (37.2%)
Hypertension	80 (41.9%)	6 (17.1%)	74 (47.4%)
Hyperlipidemia	59 (30.9%)	5 (14.3%)	54 (34.6%)
Chronic kidney disease	28 (14.7%)	2 (5.7%)	26 (16.7%)
End-stage renal disease	9 (4.7%)	0 (0.0%)	9 (5.8%)
Heart failure	32 (16.8%)	1 (2.9%)	31 (19.9%)
Coronary artery disease	48 (25.1%)	3 (8.6%)	45 (28.8%)
Atrial fibrillation	16 (8.4%)	1 (2.9%)	15 (9.6%)
COPD	19 (9.9%)	1 (2.9%)	18 (11.5%)
Outpatient Medications (90 Days Before Admission)^a			
K ⁺ -affecting medication use	90 (47.1%)	12 (34.3%)	78 (50.0%)
Etiology of Hypokalemia			
Acute K ⁺ shift	35 (18.3%)	35 (100.0%)	—
Thyrotoxic periodic paralysis	25	25	—
Sporadic periodic paralysis	7	7	—
Drug-related	3	3	—
Chronic K ⁺ deficit	156 (81.7%)	—	156 (100.0%)
Gastrointestinal disorders	47	—	47
Diuretics	35	—	35
Bartter/Gitelman syndrome	23	—	23
Alcoholism	19	—	19
Primary aldosteronism	19	—	19
Renal tubular acidosis	7	—	7
Diabetic ketoacidosis	3	—	3
Chronic licorice use	2	—	2
Ectopic ACTH secretion	1	—	1
Baseline K⁺ Measurements			
Laboratory K ⁺ (mmol/L)	2.3 [2.0-2.4]	2.2 [1.8-2.3]	2.3 [2.0-2.4]
ECG-K ⁺ (mmol/L)	2.5 [2.3-2.8]	2.4 [2.2-2.8]	2.5 [2.3-2.8]

Values are presented as median [IQR] for continuous variables and n (%) for categorical variables. Abbreviations: ACTH, corticotropin; COPD, chronic obstructive pulmonary disease; ECG, electrocardiography; K⁺, serum potassium.

^aOutpatient medication exposure within 90 days prior to admission; the K⁺-affecting medication composite includes loop diuretics, thiazide diuretics, K⁺-sparing diuretics, renin-angiotensin-aldosterone system inhibitors, β_2 agonists, insulin, systemic corticosteroids, and laxatives. A full breakdown by individual drug class is provided in Table S2.

reversal of intracellular K⁺ shift; the time $\times$ etiology interaction was highly significant in the linear mixed-effects model (lab-K⁺: likelihood ratio $\chi^2 = 67.4$, $P < 10^{-15}$; ECG-K⁺: $\chi^2 = 37.8$, $P < 10^{-9}$). The variability in correction rates within the acute group, reflected by wider 95% CIs (Fig 4), underscores the risk of overcorrection. Indeed, 2 patients with TPP (5.7% of the acute group) developed severe rebound hyperkalemia (lab-K⁺ 8.8 and 6.5 mmol/L) during the recovery phase (Fig 5). Of note, ECG-K⁺ flagged hyperkalemia 41.6 ± 14.5 minutes before the laboratory result became available. Rebound hyperkalemia was rapidly and safely reduced with acute K⁺-lowering therapy in these 2 patients.

Discussion

In this multicenter retrospective cohort study, we investigated the utility of bloodless AI-ECG in monitoring K⁺

dynamics during K⁺ supplementation in 191 patients with severe hypokalemia. Several key findings emerged. First, ECG-K⁺ and lab-K⁺ values demonstrated strong rmcrr and paralleled each other during K⁺ repletion, with ECG-K⁺ preceding lab-K⁺. Second, AI-ECG showed good to excellent diagnostic accuracy at the standard hypokalemia threshold, with the strongest discrimination in patients with acute K⁺ shift. Third, both ECG-K⁺ and lab-K⁺ showed that patients with an acute K⁺ shift exhibited markedly faster correction rates than those with chronic K⁺ deficit, reflecting the distinct underlying pathophysiology. Fourth, AI-ECG detected rebound hyperkalemia early in 2 patients with an acute K⁺ shift due to TPP.

Our study confirms the strong performance of AI-ECG in tracking potassium dynamics throughout the supplementation period. The within-patient agreement between ECG-K⁺ and lab-K⁺ was strong (rmcrr = 0.847), and ECG-K⁺ retained good to excellent rank-order

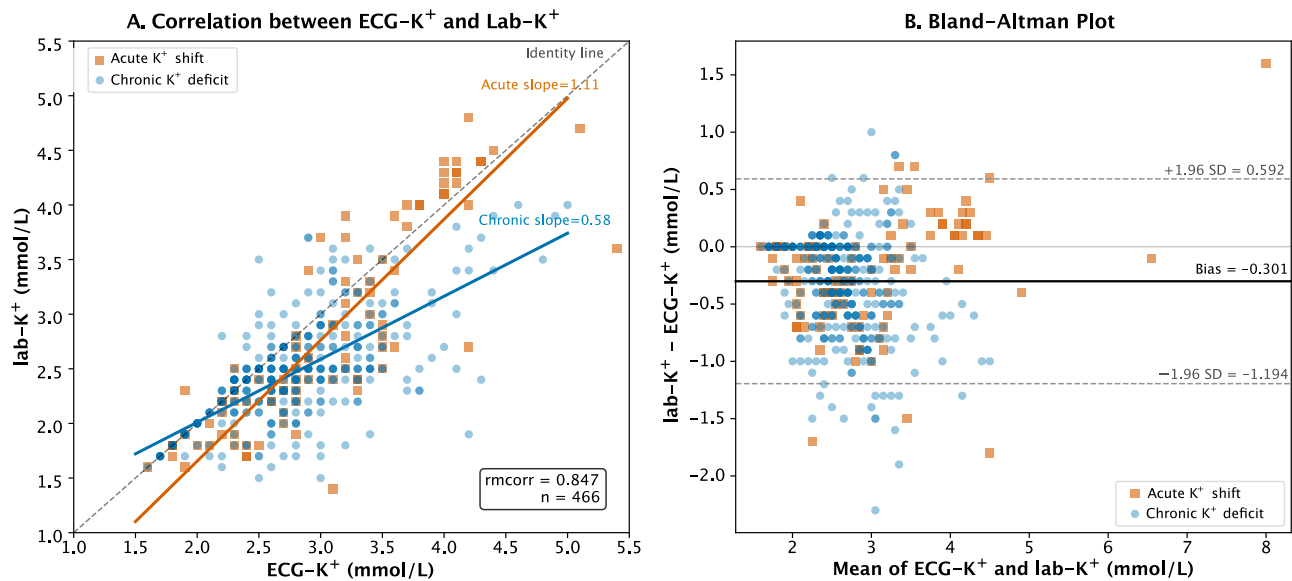


Figure 2. Correlation and agreement between paired ECG-K⁺ and lab-K⁺ levels during K⁺ supplementation for severe hypokalemia. (A) Scatterplot with mixed-effects regression lines stratified by etiology: acute K⁺ shift (orange squares, slope = 1.11) and chronic K⁺ deficit (blue circles, slope = 0.58). The dashed line indicates identity (slope = 1.0). Repeated-measures correlation (rmcorr) = 0.847. (B) Bland-Altman plot showing mean bias (lab-K⁺ minus ECG-K⁺, solid line) and 95% limits of agreement (dashed lines), stratified by etiology. Abbreviations: AI-ECG, artificial intelligence-enabled electrocardiography; ECG-K⁺, serum potassium estimated by electrocardiography; lab-K⁺, laboratory measured serum potassium.

discrimination at the standard threshold (AUC, 0.920). ECG-K⁺ therefore provides a clinically meaningful lead time over lab-K⁺ (52.5 ± 29.3 minutes), which supports its role as a proactive monitoring tool in treating severe hypokalemia.^{26,35}

A key finding was the marked difference in AI-ECG performance and K⁺ dynamics between acute K⁺ shift and chronic K⁺ deficit. First, the correlation between ECG-

K⁺ and lab-K⁺ was substantially stronger in acute cases than in chronic cases. This discrepancy likely stems from distinct pathophysiologies. Acute K⁺ shift, often caused by a rapid intracellular redistribution, generates a pronounced change in the transmembrane gradient and a clear, unambiguous ECG signal.^{36,37} Conversely, chronic K⁺ deficit involves a true total-body deficit, where the ECG signal is often subtler and confounded by baseline abnormalities

Table 2. Linear Mixed-Effects Models for the ECG-K⁺/Lab-K⁺ Relationship

	Base Model	Interaction Model
Mixed Effects		
Intercept	0.144 (SE 0.089, $P = 0.108$)	0.856 (SE 0.102, $P < 0.001$)
ECG-K ⁺ slope	0.843 (SE 0.030, $P < 0.001$)	0.577 (SE 0.036, $P < 0.001$) [chronic]
Acute (indicator)	—	-1.415 (SE 0.163, $P < 0.001$)
ECG-K ⁺ × Acute	—	+0.528 (SE 0.053, $P < 0.001$)
Random Effects		
Patient intercept variance	0.061	—
Residual variance	0.128	—
ICC	0.323	—
Model Comparison		
LR test (joint etiology effect, $df = 2$)	—	$\chi^2 = 95.4$, $P < 0.0001$
LR test (interaction term, $df = 1$)	—	$\chi^2 = 90.0$, $P < 0.0001$
Derived slopes		
Chronic K ⁺ deficit	—	0.577
Acute K ⁺ shift	—	1.105 (0.577+0.528)

The base model is $\text{lab-K}^+ \sim \text{ECG-K}^+ + (1|\text{patient})$. The interaction model adds $\text{ECG-K}^+ \times \text{etiology}$. Generalized estimating equations sensitivity analysis confirmed identical results (exchangeable $\rho = 0.284$). Abbreviations: df , degrees of freedom; ECG, electrocardiography; ICC, intraclass correlation coefficient; K⁺, serum potassium; lab-K⁺, laboratory measured serum potassium; LR, likelihood ratio; SE, standard error.

Table 3. Diagnostic Accuracy of ECG-K⁺ for Detecting Lab-K⁺ < 3.5 mmol/L by Etiology

Group	n	Patients	AUC-ROC (95% CI) ^a	Sens ^b	Spec ^b	PPV	NPV
Overall	466	191	0.920 (0.863-0.961)	0.912	0.761	0.972	0.486
Acute K ⁺ shift	94	35	0.952 (0.900-0.993)	0.894	0.857	0.937	0.774
Chronic K ⁺ deficit	372	156	0.870 (0.741-0.959)	0.915	0.611	0.979	0.268

Abbreviations: AUC-ROC, area under the receiver operating characteristic curve; K⁺, serum potassium; ECG-K⁺, serum potassium estimated by electrocardiography; lab-K⁺, laboratory measured serum potassium; NPV, negative predictive value; PPV, positive predictive value.

^aAUC 95% CI computed by patient-level clustered bootstrap (5,000 resamples) to account for within-patient correlation.

^bSensitivity and specificity at the fixed threshold defined in the table title.

(eg, left ventricular hypertrophy) or concurrent electrolyte imbalances like hypomagnesemia, creating a complex “composite signal” that challenges the AI model.³⁸⁻⁴⁰ Second, these underlying physiological differences were also reflected in the treatment response. The correction rate was nearly 3-fold faster in acute cases (0.121 mmol/L/h in acute K⁺ shift vs 0.039 mmol/L/h in chronic K⁺ deficit). This rapid correction reflects the reversal of the intracellular shift whereas the slower rate in chronic cases corresponds to the gradual replenishment of a total-body deficit.⁴¹ Together, these findings underscore the utility of AI-ECG as a real-time monitoring tool that can provide crucial insights into patient-specific pathophysiology and treatment response between intermittent blood draws.⁴²

Rebound hyperkalemia is a potential complication of K⁺ therapy for hypokalemia. This life-threatening condition is a well-recognized risk, particularly in patients with acute, shift-related hypokalemia such as with TPP.^{34,37,41} In our cohort, AI-ECG successfully facilitated the early detection of severe rebound hyperkalemia in 2 patients with TPP, but no such events were observed in the chronic K⁺ deficit group. A recent pragmatic randomized controlled trial demonstrated that AI-ECG dyskalemia alerts led to significantly earlier physician

intervention for ECG-detected hyperkalemia.⁴³ Given that a K⁺ surge can occur unpredictably during therapy for acute K⁺ shift, bloodless AI-ECG monitoring with automated alerts may offer a strategy for the rapid recognition and management of rebound hyperkalemia.

This study has several limitations. First, the retrospective, predominantly single-center design entails nonstandardized treatment timing and limits generalizability across health care settings, ECG hardware platforms, and to non-Asian populations. Second, exclusion of approximately half the screened patients without follow-up measurements introduces potential selection bias. Third, in-hospital medication exposure during the K⁺ correction window was not systematically captured for direct adjustment. Fourth, AI-ECG monitoring is applicable only to patients in whom the initial ECG-K⁺ also flags hypokalemia (ECG-K⁺ < 3.5 mmol/L), limiting its real-world applicability. Finally, long-term accuracy and clinical outcomes were not assessed; AI-ECG should be regarded as a real-time monitoring adjunct rather than a standalone decision tool. Prospective studies in multi-ethnic populations with predefined timing protocols are warranted.

This study demonstrates that AI-ECG may provide clinically meaningful real-time monitoring of serum K⁺

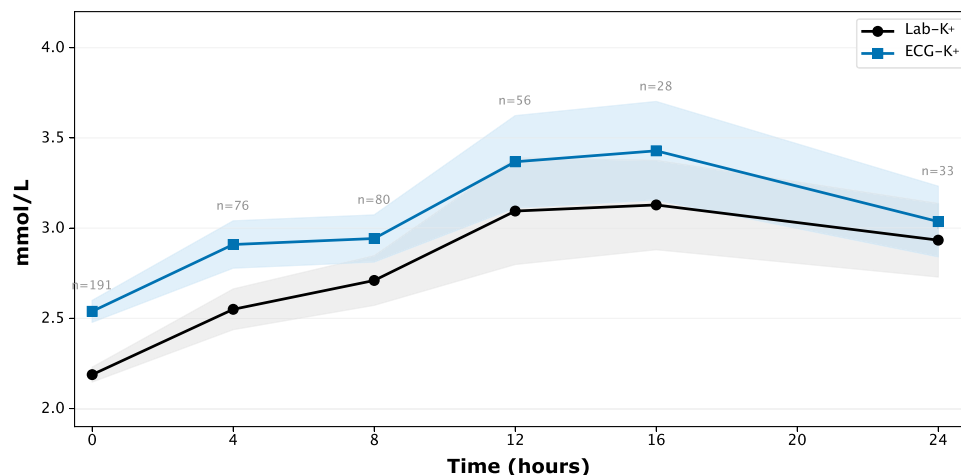


Figure 3. Changes in paired lab-K⁺ and ECG-K⁺ levels during K⁺ supplementation. Dynamic changes in lab-K⁺ (black line) and ECG-K⁺ (blue line) levels over 24 hours of K⁺ supplementation therapy are shown for patients with severe hypokalemia (initial K⁺ ≤ 2.5 mmol/L). Shaded areas represent 95% CI. Abbreviations: ECG-K⁺, serum potassium estimated by electrocardiography; lab-K⁺, laboratory measured serum potassium.

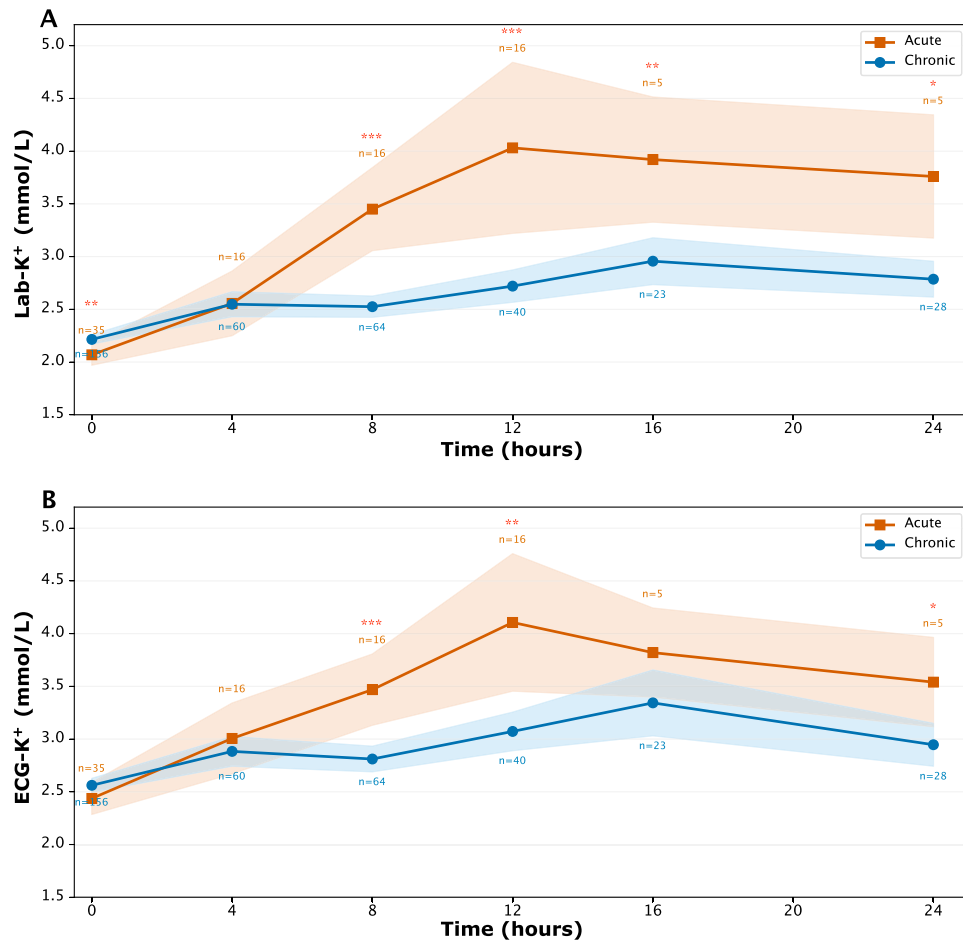


Figure 4. Temporal dynamics of ECG-K⁺ and lab-K⁺ over 24 hours in hypokalemia patients. The temporal changes in K⁺ levels in patients with severe hypokalemia (initial K⁺ ≤ 2.5 mmol/L) are stratified by etiology (acute vs chronic) during the first 24 hours of K⁺ supplementation therapy. (A) Trends of lab-K⁺ values. (B) Trends of ECG-K⁺ values. Sample sizes (n) are shown for each time point. Statistical significance between acute and chronic groups is indicated by asterisks: **P* < 0.05, ***P* < 0.01, ****P* < 0.001, Mann-Whitney *U* test. Abbreviations: ECG-K⁺, serum potassium estimated by electrocardiography; lab-K⁺, laboratory measured serum potassium.

dynamics during the treatment of severe hypokalemia, with the strongest performance in patients with an acute K⁺ shift. By enabling personalized, responsive K⁺

replacement strategies, ECG-K⁺ monitoring may hold the potential to reduce the cardiovascular risks associated with severe hypokalemia and its treatment.

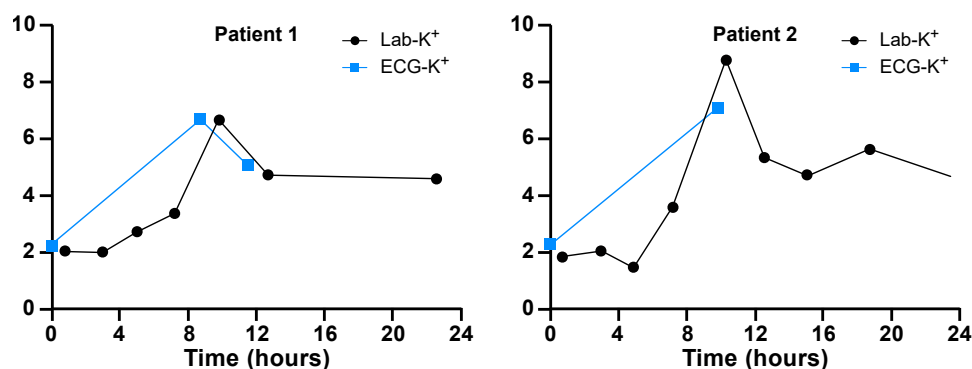


Figure 5. Early detection of rebound hyperkalemia by ECG-K⁺ in 2 patients with thyrotoxic periodic paralysis. These representative cases show the temporal changes in lab-K⁺ (black circles) and ECG-K⁺ (blue squares) during K⁺ supplementation therapy. Abbreviations: ECG-K⁺, serum potassium estimated by electrocardiography; lab-K⁺, laboratory measured serum potassium.

Supplementary Material

Supplementary File (PDF)

Figure S1: Visualized AI-ECG based analysis for hypokalemia in a 12-lead ECG format.

Figure S2: Bootstrap distribution of OLS regression coefficients (5,000 resamples).

Figure S3: ROC curves for detecting lab-K⁺ < 3.5 mmol/L, stratified by hypokalemia etiology: AUC values with patient-level clustered bootstrap 95% CIs.

Item S1: Supplementary methods: mixed-effects model specification, GEE working correlation structure selection, and clustered bootstrap ROC methodology.

Table S1: Comparison of baseline characteristics between included (n = 191) and excluded (n = 222) patients.

Table S2: Outpatient K⁺-affecting medication use by etiology (descriptive only; not a confounder substitute for missing admission-time medication data).

Table S3: Discrepancy analysis between ECG-K⁺ and lab-K⁺ measurements at 2 thresholds (>0.5 and >1.0 mmol/L).

Table S4: GEE sensitivity analysis under 3 working correlation structures (independence, exchangeable, and AR(1)) with QIC comparison, ICC, and baseline-only correlation.

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