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The diagnostic value of T-wave to R–wave amplitude ratio on electrocardiogram in the diagnosis of hyperkalemia

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Abstract: **Objective:** The aim of this study is determining the diagnostic value of the T-wave to R–wave amplitude ratio (T/R ratio) in the electrocardiogram (ECG) at the time of admission in terms of the diagnosis of hyperkalemia in patients who are at risk for hyperkalemia who apply to the emergency department (ED).

Methods: This cross-sectional study was conducted with patients over 18 years of age who presented to the ED and have an estimated glomerular filtration rate (eGFR) below 60ml/min/1.73m^2. The patients were divided into 2 groups according to the potassium value; hyperkalemia and normokalaemia groups. T/R ratios were measured on the ECG. All measurements were made in these precordial leads; V2, V3, and V_T highest (is defined as precordial lead where the T wave is measured the highest).

Results: A total of 345 patients with low eGFR were included. Hyperkalemia was detected in 115 (33.3%) of these patients, while 230 patients (66.6%) were in the normokalaemia group. T wave amplitude and T/R ratio were found to be statistically significantly increased in the hyperkalemia group in all leads (V2, V3, and V_T highest). Area under the curve (AUC) values are 0.778 for T/R ratio and 0.717 for T wave amplitude.

Conclusion: The presence of increased T/R ratio in the ECG of patients with known low eGFR may be more helpful for the diagnosis of hyperkalemia than the classical hyperkalemia ECG findings.

Keywords: ECG; Emergency Department; Hyperkalemia, T/R Ratio

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1. Introduction

Hyperkalemia is a common electrolyte disorder that can be life-threatening if not recognized and treated promptly. A serum plasma potassium concentration greater than 5.5 mEq/L is defined as hyperkalemia, and mortality and morbidity due to hyperkalemia are higher in patients with chronic kidney disease, hypertension, coronary artery disease, and related conditions (1-3). In addition, many hyperkalemic patients, especially those with chronic kidney disease, are clinically asymptomatic and may experience cardiotoxic effects, leading to serious arrhythmias and even death (4). Therefore, early detection of cardiotoxic effects caused by hyperkalemia is very important.

Electrocardiogram (ECG) is the most widely used diagnostic method to evaluate cardiac involvement in hyperkalemic patients, and various ECG findings associated with hyperkalemia in large series have been reported including: peaked T waves, prolonged QRS complexes, diminished P waves, and prolonged PR intervals (5-7). However, in clinical practice, the success of physicians in predicting the presence of hyperkalemia by evaluating these ECG findings alone has been shown to be quite low and variable (8,9).

In recent years, several studies have reported that T-wave to R-wave amplitude ratio (T/R ratio) is more specific than the classic findings of hyperkalemia on the ECG, especially when the plasma potassium level is above 6 mEq/L (10-13). Another study found a significant correlation between serum potassium concentrations and T/R ratios in patients with end-stage renal disease (14). However, the results of the existing studies are not consistent, and the diagnostic value of T/R ratio in hyperkalemia is still unclear.

The aim of this study was to determine the diagnostic value of the T/R ratio on the ECG at the time of admission for the diagnosis of hyperkalemia in patients at risk of hyperkalemia presenting to the emergency department (ED).

2. Methods

2.1. Study design

This cross-sectional study was conducted on patients over 18 years of age who presented to the ED during a period of 4 months between 10/01/2021 and 02/01/2022 and who were considered potentially at risk for hyperkalemia with a eGFR below 60ml/min/1.73 m^2. Ethical approval was obtained from the local ethics committee before the start of the study. The ethical approval code is: 2012-KAEK-15/2360.

2.2. Study participants

During the study period, patients over 18 years of age who presented to the ED for any reason and had a eGFR less than 60 ml/min/1.73 m^2 and were considered potentially at risk for hyperkalemia were consecutively enrolled in the study. The eGFR value of the patients included in the study was determined below 60 ml/min/1.73m^2 based on previous studies on the relationship between decreased renal function and serum potassium levels (15). Patients with hemolysis in the blood sample, pregnant patients, patients with paced rhythm, left bundle branch block, left ventricular hypertrophy, sine wave pattern, patients diagnosed with acute coronary syndrome, and patients recovering from cardiac arrest were excluded from the study. The remaining patients were divided into 2 groups according to potassium level; those with potassium level of 5.5 mEq/L and above were included in the hyperkalemia group, and those below 5.5 mEq/L were included in the normokalemia group.

2.3. Study protocol and ECG analysis

All demographic and clinical characteristics of the patients selected for the study were reviewed by the investigators. The laboratory values obtained on admission and the patients' initial ECGs were recorded on a digital system for later re-evaluation in the patient's study form. All ECGs were digitized and accurate computer-assisted reading was performed using the latest version of Adobe Photoshop. In this evaluation, heart rate, P wave amplitude and width, PR interval, QT interval, corrected QT (QTc) interval, QRS width, T wave amplitude, R wave amplitude and T/R ratio were calculated. While evaluating the ECG, measurements were made in these precordial leads: V2, V3, and V_T highest (defined as precordial lead where the T wave is measured the highest). The cases where the T wave amplitude is above 10 mm are considered as T wave peaks. The evaluation of ECGs was based on the guideline published by the American Heart Association (16).

2.4. Sample size calculation

The sample size of this study was calculated using G-Power for Mac OS X (version 3.1.9.2; University of Düsseldorf, Germany). Considering that the prevalence of hyperkalemia in patients with eGFR less than 60 mL/min/1.73 m^2 was reported to be 40% in a previous study by Moranne et al. and accepting a type 1 error level of 5% according to the 90% sensitivity target value, the total sample size of the study was calculated to be at least 335 patients, of whom 225 were in the normokalemia group and 110 were in the hyperkalemia group (17).

2.5. Statistical analysis

All data obtained during the study and recorded in the study form were analyzed using the IBM SPSS 20.0 (Chicago, IL, USA) statistical program. Histogram, Q-Q plot, and Shapiro-Wilk test were used to evaluate whether the distribution of discrete and continuous numerical variables was suitable for normal distribution. Descriptive statistics are presented as mean±standard deviation (SD) or median (25-75% interquartile range (IQR)) for discrete and continuous numerical variables and as number of cases and (%) for categorical variables.

Categorical variables were evaluated using chi-squared, and continuous variables were evaluated using t-test or Mann-Whitney U test. To calculate the diagnostic value of the T/R ratio for the diagnosis of hyperkalemia, ROC analysis was performed and the area under the curve (AUC) was calculated. The best of the cut-off value for the T/R value was determined using the Youden-J index (14). The 95% confidence intervals (95% CIs) were also calculated when appropriate, and a P-value less than 0.05 was considered statistically significant.

3. Results

During the study period, 465 patients with low eGFR were consecutively enrolled. 120 of these patients were excluded for various reasons. After exclusion, a total of 345 patients remained for statistical analysis. Of these patients, 200 (58%) were female and 145 (42%) were male. Hyperkalemia was detected in 115 (33.3%) of these patients, while 230 patients (66.6%) were in the normokalemia group. The flow chart of the patients is shown in figure1. The basic demographic and clinical characteristics of the patients according to the groups are summarized in table1.

When the groups were compared in terms of basic ECG characteristics, it was found that the QRS width was significantly wider in the hyperkalemia group, while no difference was found in terms of QT, QTc duration and PR intervals. In both groups, V_T highest was most frequently detected in leads V2 and V3 (Table 2).

While T-wave amplitude and T/R ratio were found to be statistically significantly increased in the hyperkalemia group in all leads (V2, V3, and V_T highest), R-wave amplitude was found to be statistically decreased in the hyperkalemia group in leads V2 and V_T highest. There was no difference in R-wave amplitude in lead V3 (Table 3).

ROC analysis was performed and the AUC was calculated to evaluate the diagnostic efficacy in predicting hyperkalemia (>5.5 mEq/L) for T/R ratio, T and R wave amplitudes, and width of QRS complex all in leads V2, V3, and V_T highest. However, it was not reported because the AUC value of the T/R ratio of leads V2 and V3 was calculated to be less than 0.70. (Figures 2a-2d)

The AUC values for T/R ratio and T-wave amplitude in lead V_T highest were respectively 0.778 (95% CI: 0.727,0.829) and 0.717 (95% CI: 0.659,0.775) (Table 4). For the prediction of hyperkalemia, the sensitivity/specificity values for the different cut-off points are shown in table 5, together with the best cut-off value for the T/R ratio on the V_T highest lead, which has the best AUC value among all variables.

Table 1 Patients' demographical and clinical characteristics were presented according to groups

	Normokalaemia group (n=230)	Hyperkalemia group (n=115)	P-value
Age, Median (IQR 25%-75%)	76 (68-84)	72 (62-81)	**0.004**
Sex, n (%)			
• Female	146 (63.5%)	54 (47%)	**P<0.001**
• Male	84 (36.5%)	61 (53%)	
Comorbidities, n (%)			
• Hypertension	157 (67.4%)	76 (32.6%)	0.684
• Diabetes mellitus	69 (52.7%)	62 (47.3%)	**P<0.001**
• Coroner artery disease	72 (31.3%)	34 (29.6%)	0.741
• Heart failure	30 (13%)	22 (19.1%)	0.136
• Chronic renal failure	41 (17.8%)	33 (28.7%)	**0.02**
• Chronic obstructive pulmonary Disease (COPD)	25 (10.9%)	16 (13.9%)	0.41
• Cerebrovascular disease	12 (5.2%)	6 (5.2%)	1
Medications, n (%)			
• Loop diuretic	36 (15.7%)	29 (25.2%)	**0.032**
• Thiazide diuretic	55 (25.9%)	24 (20.9%)	0.526
• K+ sparing diuretic	5 (2.2%)	9 (7.8%)	**0.012**
• Oral antidiabetic	56 (24.3%)	35 (30.4%)	0.226
• Angiotensin-converting enzyme (ACE) inhibitor	57 (24.8%)	12 (10.4%)	**0.002**
• Angiotensin receptor blocker (ARB)	53 (23%)	22 (19.1%)	0.406
• Beta blocker	72 (31.3%)	28 (24.3%)	0.179
• Acetylsalicylic acid	81 (35.2%)	33 (28.9%)	0.225
• Calcium channel blocker	60 (34.8%)	40 (26.1%)	0.093
• Insulin	14 (6.1%)	24 (20.9%)	**p<0.001**
• Digoxin	4 (1.7%)	1 (0.9%)	0.668
Laboratory parameters, Median (IQR 25%-75%)			
• Urea (mg/dL)	58 (44-85)	95 (63-161)	**P<0.001**
• Creatinine (mg/dL)	1.43 (1.2-2.08)	2.31 (1.43-5.57)	**P<0.001**
• Estimated glomerular filtration rate (eGFR) (mL/min/1.73 m^2)	39.5 (25.1-47.6)	25.6 (9.8-41.5)	**P<0.001**
• Sodium (mEq/L)	137 (135-139)	136 (131-139)	**0.015**
• Potassium (mEq/L)	4.4 (4-4.83)	6.06 (5.7-6.61)	**P<0.001**
• Chlor (mmol/L)	103 (99106)	103 (98-108)	0.383
• Calcium (mg/dL)	9 (8.6-9.4)	8.8 (8.5-9.3)	**0.042**
• Albumin (g/L)	3.79 (3.42-4.1)	3.5 (3.13-3.9)	**P<0.001**
• pH	7.38 (7.34-7.42)	7.28 (7.17-7.34)	**P<0.001**
• Partial pressure of carbon dioxide (PCO2) (mmHg)	38.9 (34.5-43.2)	39.3 (32.1-48)	0.497
• Bicarbonate (HCO_3) (mmol/L)	22.4 (20.1-24.6)	17.7 (13.9-21.9)	**P<0.001**
• Base deficit (mmol/L)	-1.4 (-4.37-0.4)	-7.2 (-14.5 - -3)	**P<0.001**
• Lactate (mmol/L)	1.66	2.11 (1.24-4.3)	**0.003**

IQR: Interquartile range

Table 2 Patients' ECG characteristics according to groups

ECG Parameters, Median (IQR 25%-75%)	Normokalaemia groups	Hyperkalemia groups	P-value
• Heart rate (beats/min)	86 (73-99)	89 (76-104)	0.268
• PR interval (ms)	166 (146-190)	174 (148-196.5)	0.444
• QRS width (ms)	90 (82-100.5)	100 (86-116)	**<0.001**
• QT intervals (ms)	366 (342-400)	374 (344-400)	0.437
• QTc (ms)	413 (395.7-431.25)	418 (397-438)	0.066
Precordial lead where V_T highest is observed			
• V1	1 (0.4%)	0 (%0)	
• V2	81 (35.2%)	45 (39.1%)	
• V3	56 (24.3%)	41 (35.7%)	0.065
• V4	21 (9.1%)	10 (8.7%)	
• V5	44 (19.1%)	12 (10.4%)	
• V6	27 (11.7%)	7 (6.1%)	

ms: Millisecond; IQR: Interquartile range

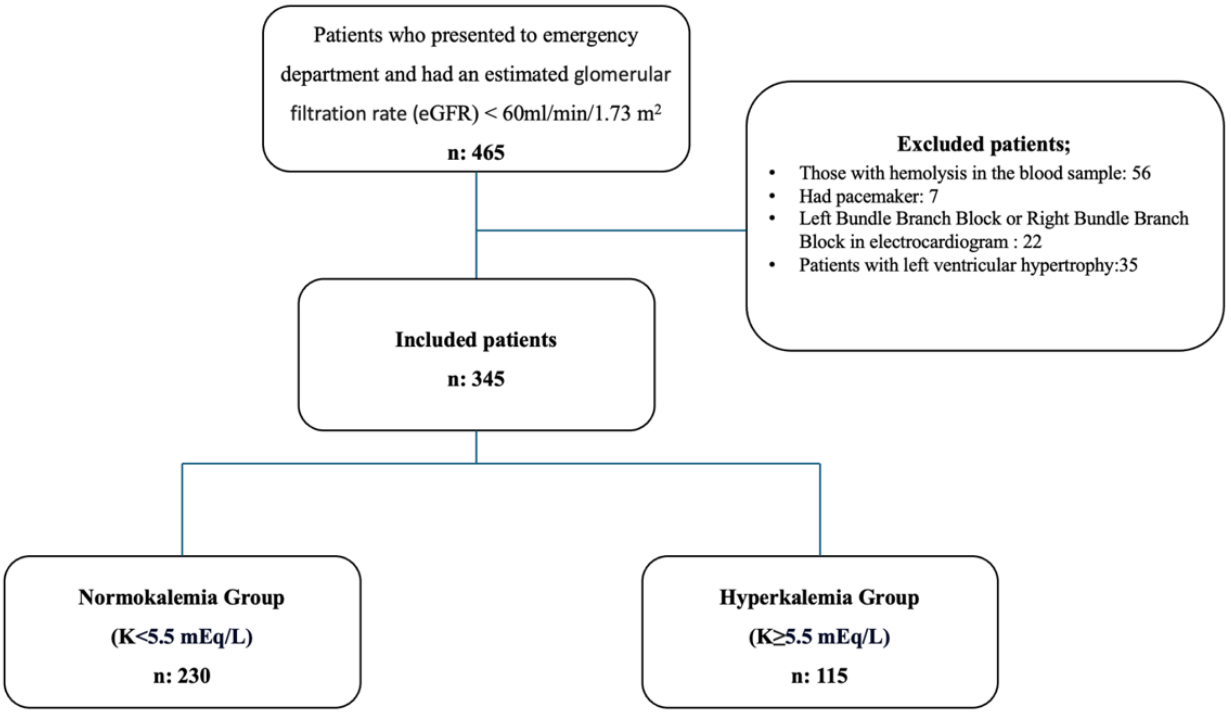

Figure 1 Flowchart of the study

Table 3 T and R wave amplitudes and T/R ratios in leads V2, V3, and V_T highest according to groups

ECG lead	Normokalaemia group	Hyperkalemia group	P-value
V_2 lead, Median (IQR 25%-75%)			
• T amplitude (mm)	2.3 (1.4-3.5)	3.2 (2.0-4.7)	**P<0.001**
• R amplitude (mm)	3.6 (2.15-6.4)	2.9 (1.8-5.1)	**P<0.001**
• T/R ratio	0.58 (0.35-1.1)	1.0 (0.56-1.7)	**P<0.001**
V3 lead, Median (IQR 25%-75%)			
• T amplitude (mm)	2.3 (1.5-3.25)	3.4 (2.2-5.1)	**P<0.001**
• R amplitude (mm)	3.5 (2.25-5.7)	3.5 (2.1-6)	0.931
• T/R ratio	0.61 (0.38-1)	0.94 (0.46-1.84)	**P<0.001**
V_T highest lead, Median (IQR 25%-75%)			
• T amplitude (mm)	3.1 (2.3-4.3)	4.7 (3.3-6.5)	**P<0.001**
• R amplitude (mm)	6.15 (3.9-9.1)	4.4 (2.8-6.1)	**P<0.001**
• T/R ratio	0.5 (0.30-0.77)	1.0 (0.71-1.68)	**P<0.001**

mm: Millimeter; IQR: Interquartile range

Table 4 Prognostic values of T/R Ratio and T wave amplitude to predict hyperkalemia in lead V_T highest

Parameter	T/R ratio	T wave amplitude
Area Under Curve (AUC) (95% Cl)	0.778 (0.727,0.829)	0.717 (0.659,0.775)
Best cut-off value*	0.7143	4.4 mm
Sensitivity (95% CI)	75.65 (66.77,83.17)	57.39 (47.83,66.56)
Specificity (95% Cl)	72.17 (65.9,77.86)	77.39 (71.43,82.63)
Positive likelihood ratio (PLR) (95% Cl)	2.72 (2.16,3.43)	2.54 (1.91,3.38)
Negative likelihood ratio (NLR) (95% Cl)	0.34 (0.24,0.47)	0.55 (0.44,0.69)
Accuracy (95% Cl)	73.33 (68.33,77.93)	70.72 (65.61,75.48)

*: The best of cut-off value was decided using the Youden-J index; AUC: Area under curve; PLR: Positive likelihood ratio; NLR: Negative likelihood ratio

4. Discussion

Our study found that in patients with reduced GFR presenting to the ED, T/R ratio is more accurate (higher AUC) in diagnising hyperkalemia as compared to other ECG parameters, such as QRS width and T-wave amplitude.

Hyperkalemia presents as a serious electrolyte disorder in

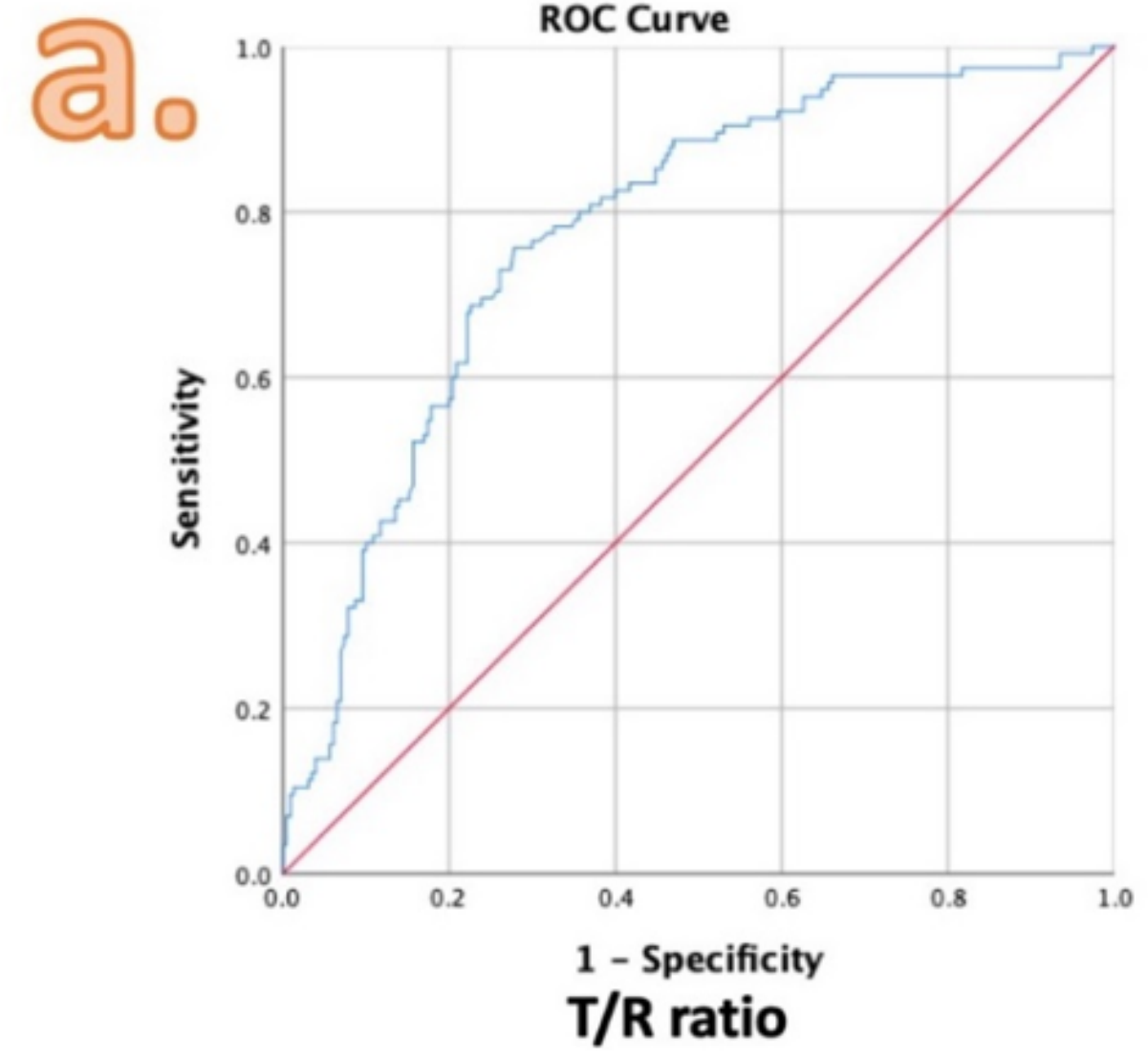

Figure 2a ROC graph for T-wave to R–wave amplitude ratio (T/R ratio)

Table 5 The sensitivity and specificity values for different cut-off points for T-wave to R–wave amplitude ratio (T/R ratio)

Different T/R ratio values	Sensitivity (%)	Specificity (%)	NLR (Negative likelihood ratio)	PLR (Positive likelihood ratio)	Accuracy
0.4784	90.43 (83.53,95.13)	46.52 (39.94,53.13)	0.21 (0.12,0.37)	1.69 (1.48,1.93)	61.16 (55.79,66.33)
0.7143	75.65 (66.77,83.17)	72.17 (65.9,77.86)	2.72 (2.16,3.43)	0.34 (0.24,0.47)	73.33 (68.33,77.93)
0.9167	57.39 (47.83,66.56)	80 (74.24,84.97)	0.53 (0.42,0.66)	2.87 (2.12,3.88)	72.46 (67.43,77.11)

the emergency department. Because of its cardiac effects, prompt recognition and treatment of potassium disorders is of great importance. To date, many studies have been conducted on the ECG to determine its value in the diagnosis of hyperkalemia. The first major study investigating the sensitivity and specificity of ECG in predicting hyperkalemia was conducted by Wrenn et al (8). ECG findings of hyperkalemia were defined as increase in T-wave amplitude, decrease in P-wave amplitude, and QRS complex prolongation, and physicians were asked to evaluate ECGs of patients at risk for hyperkalemia, blinded to potassium levels. The sensitivity of ECG findings in predicting hyperkalemia was found to be 62%, while the specificity was found to be 85% at plasma potassium levels above 6.5 mEq/L. On the other hand, in a retrospective study by Regolisti et al. examining T-wave changes in patients with acute kidney injury, it was reported that ECG changes were present in approximately half of 168 patients with plasma potassium levels above 6 mEq/L, and the most common finding of these ECG changes were T-wave spikes at 34% (9). However, ECG changes have been found

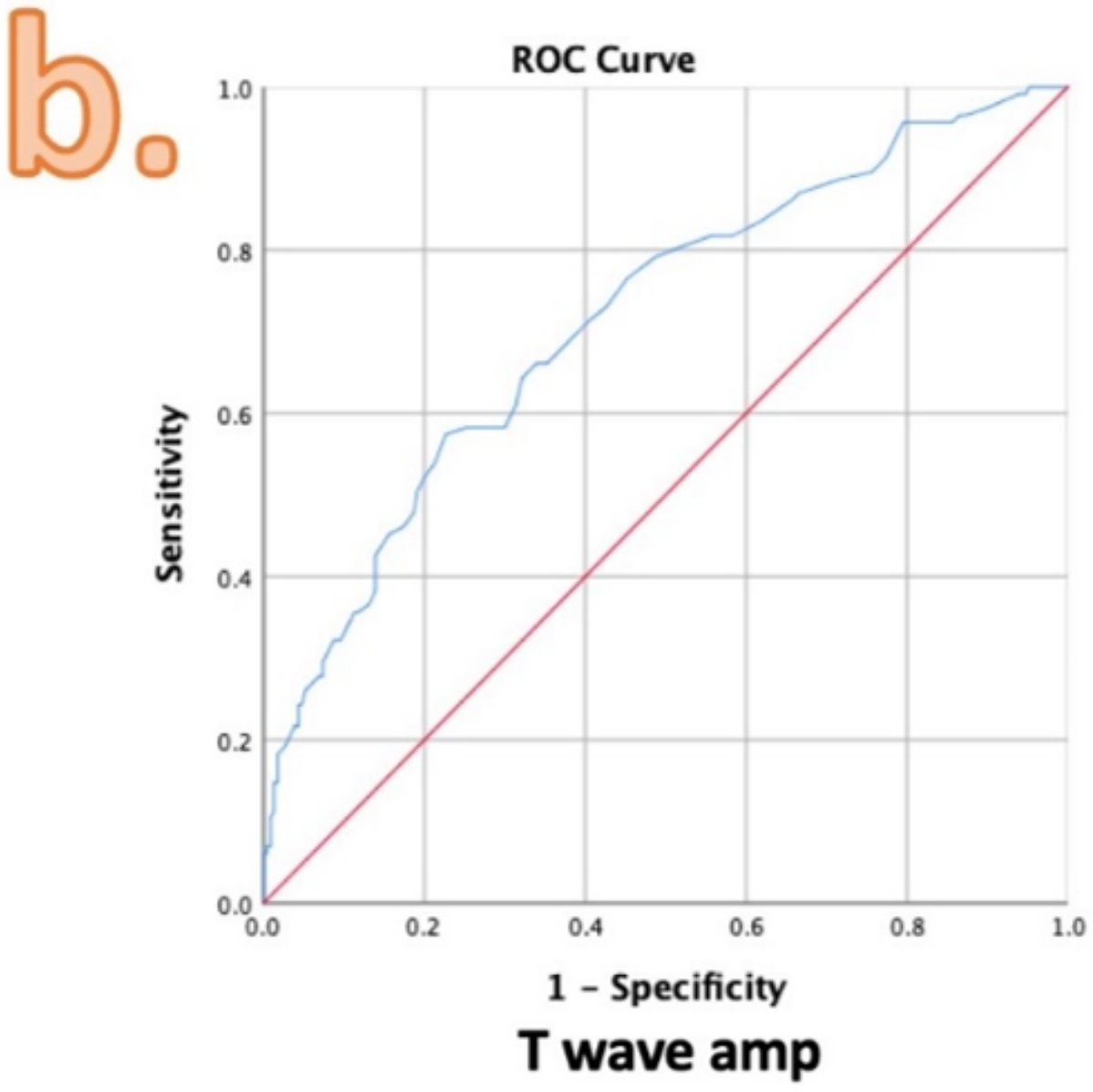

Figure 2b ROC graph for T-wave amplitude

to be a poor predictor of serum potassium levels in patients with acute kidney injury. In our study, a statistically significant difference in T-wave amplitudes was found between the normokalemia and hyperkalemia groups. However, considering that the AUC value for T wave amplitude was 0.717 (95% CI: 0.659,0.775), the sensitivity was 57.39%, and the specificity w as 7 7.39%, i t d oes n ot s eem p ossible t o s ay t hat it alone is a strong predictive factor in the diagnosis of hyperkalemia.

In addition to T-wave peaks, there are several other ECG findings associated with hyperkalemia in classic sources. Some of them are: PR interval prolongation, QT interval shortening, P wave flattening, QRS complex widening and QRS complex worsening in a sinusoidal pattern. In the study by Regolisti et al., patients were divided into two groups according to their serum potassium levels. Of these, those with a plasma potassium level above 5.5 mEq/L were included in the hyperkalemia group and those below 5.5 mEq/L were included in the control group. No statistically significant difference was found between the ECGs of these two groups in terms of QRS duration, QT interval, and QTc duration (4). In our study, similar to the study by Regolisti et al., we did not find any difference between the groups with plasma potassium levels above and below 5.5 mEq/L in terms of PR interval, QT interval, and QTc duration. However, in contrast to Regolisti's study, a significant difference in QRS duration was observed between the hyperkalemic and normokalemic groups in our study. However, given that the AUC is below

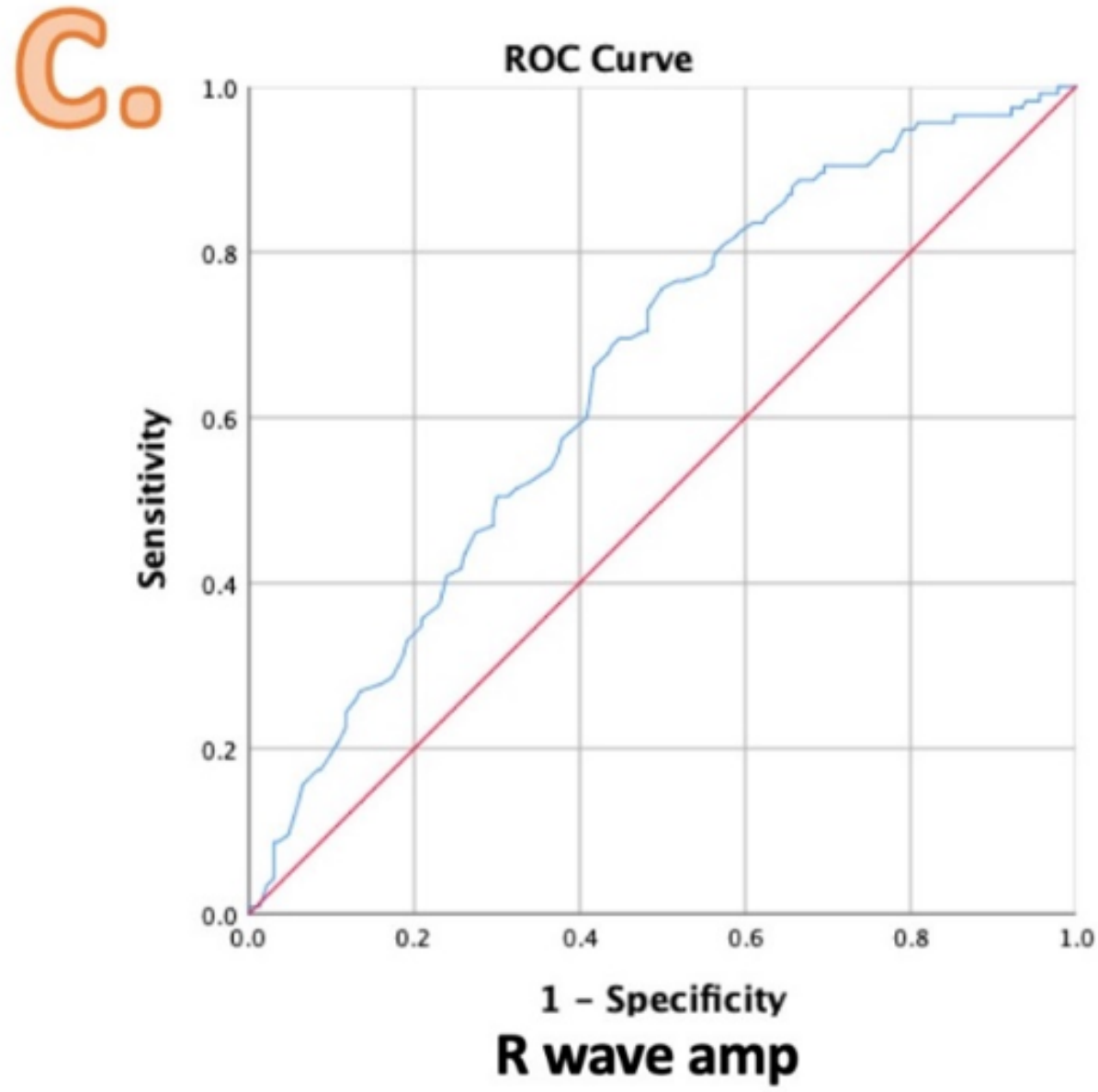

Figure 2c ROC graph for R-wave amplitude

0.70, it is unlikely to be used in routine practice for the diagnosis of hyperkalemia.

Another parameter that has been associated with hyperkalemia in recent years is the T/R ratio, which is expressed as the ratio of T-wave amplitude to R-wave amplitude. Because the expected effect of hyperkalemia is an increase in T-wave amplitude and a decrease in R-wave amplitude, the T/R ratio has been the subject of research to minimize other confounding factors. Buerschaper et al. performed an ECG study to predict pre- and post-transplant events in patients with chronic kidney disease (14). 139 patients awaiting transplantation were enrolled in the study and their ECGs were evaluated. The increase in T/R ratio in the anterior leads (V2-V4) before transplantation was found to be predictive of increased cardiovascular disease within 1 year after transplantation. Multivariate cox regression analysis; showed that an increase in T/R ratio in the anterior and inferior leads (II, III, and aVF) was associated with cardiovascular events. This suggests that hyperkalemia and arrhythmias due to hyperkalemia also cause cardiovascular events. In addition, a significant correlation was found between T/R ratio and potassium levels.

A study by Aslam et al. investigated the reliability of ECG in detecting hyperkalemia in hemodialysis patients (10). T-wave amplitude and T/R ratio were calculated in the precordial leads, and no significant difference was found between the hyperkalemic and normokalemic groups. In another study, Green et al. investigated the relationship of T-wave changes and T/R ratio with serum potassium levels in patients with end-stage renal disease (11). During ECG mea-

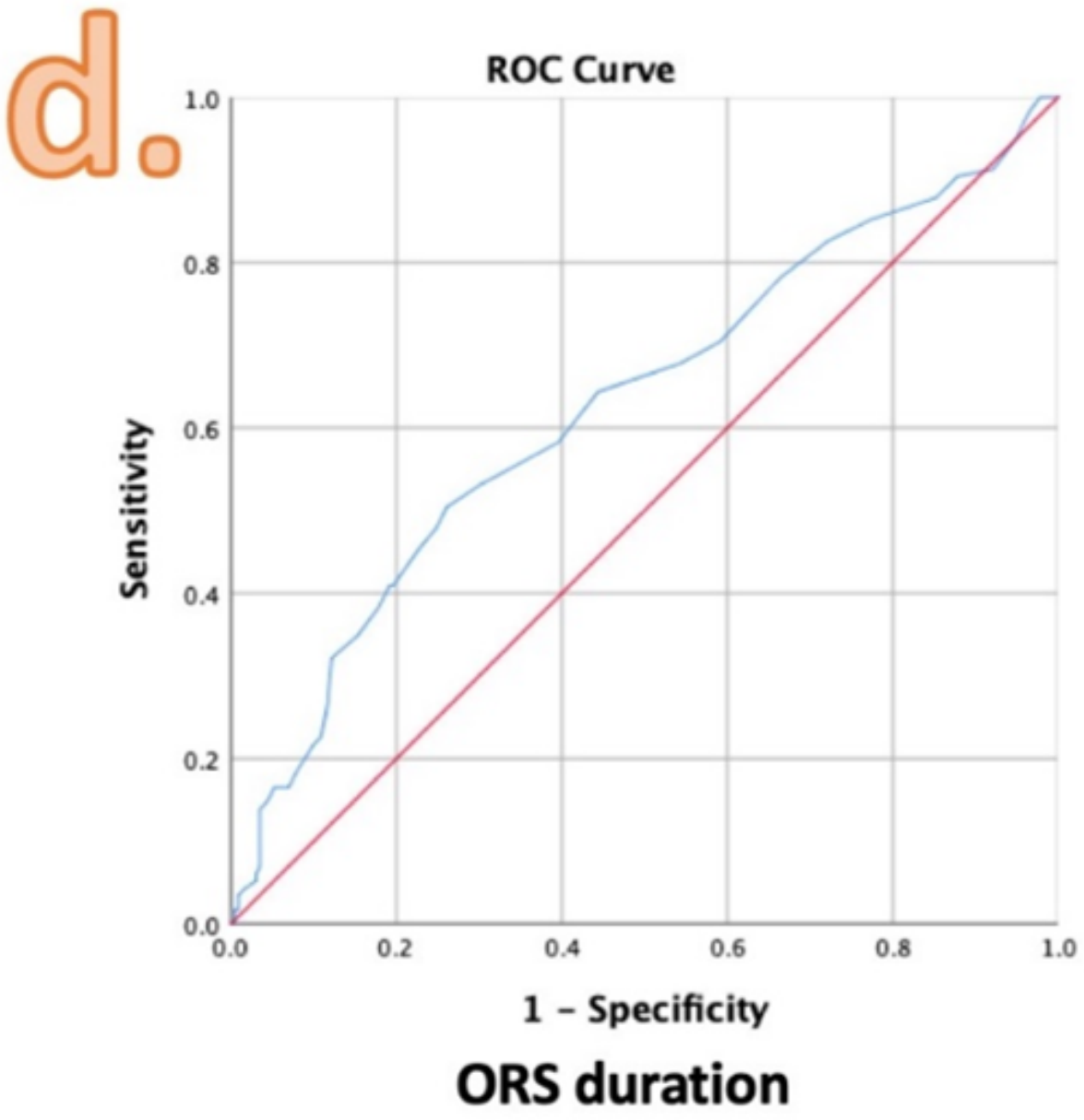

Figure 2d ROC graph for QRS complex duration

surements, the longest T wave and the highest R wave in any lead in the same cardiac cycle were related to each other, and an increased T/R ratio above 0.75 was determined. The increased T/R ratio was found to have a specificity of 85% and a sensitivity of 24% for cases in which the serum potassium level is above 6 mEq/L, and it was emphasized that it is a more specific finding than the T wave peak. Another study by Montague et al. retrospectively analyzed ECG findings in hyperkalemia (12). 90 patients with a plasma potassium level above 6 mEq/L were included in the study. Measurements were made in lead V4 and in the lead with the maximum amplitude of the R wave. In both measurements, the T/R ratio increased significantly as a function of potassium levels, but its diagnostic use was limited.

Cardiovascular disease is the leading cause of morbidity and mortality in patients with chronic kidney disease, and arrhythmias are the leading cause of these conditions. In particular, hyperkalemia is an important risk factor for arrhythmias in these patients. For this reason, regular measurement of plasma potassium levels throughout the year is recommended in patients with chronic kidney disease. Current guidelines recommend routine potassium measurement at least 1-2 times per year in patients with CKD stages 1-3 and at least 2-4 times per year in patients with CKD stages 4-5. In addition, it is emphasized that potassium levels should be remeasured within 3 days for those with potassium levels of 5.5-5.9 mEq/L and within 1 day for those with 6.0-6.4 mEq/L (19). This situation adds cost and workload to the

healthcare system and can have a negative psychosocial impact on people with chronic kidney disease. Instead, we believe that it is an important question whether ECG, which is a non-invasive, inexpensive, easily accessible and rapidly reproducible test, can be used as a more convenient alternative for both healthcare professionals and patients in the follow-up of hyperkalemia.

As a result, we believe that it stands out as a potential candidate for the follow-up of hyperkalemia, especially since the T/R ratio has the largest AUC value among the ECG parameters in our study. However, since the calculated AUC value for the diagnosis of hyperkalemia is 0.778, it is not possible to say that it is an ideal diagnostic test. However, we believe that higher sensitivity or specificity values can be obtained with different thresholds for the T/R ratio and can be used in clinical practice to exclude the diagnosis of hyperkalemia with high sensitivity values.

5. Limitations

Our study is a cross-sectional study conducted in a single center. Therefore, it may represent a limited sample. In addition, a serum potassium level above 5.5 mEq/L was considered hyperkalemia in our study. In our study, hyperkalemia levels were not graded. We believe that different results may be obtained, especially if the higher potassium levels, where cardiac effects occur, are taken as a sample.

6. Conclusion

The presence of an increased T/R ratio on ECG in patients with known low eGFR may be more helpful in the diagnosis of hyperkalemia than the classic hyperkalemic ECG findings.

7. Declarations

7.1. Acknowledgement

None.

7.2. Authors' contribution

Conceived and Designed the experiments: all authors; Performed the experiments: all authors; Analyzed and Interpreted the data: ŞKÇ, YÇ, EE; Contributed reagents, materials, analysis tools or data: all authors; Wrote the paper: ŞKÇ.

7.3. Conflict of interest

None.

7.4. Funding

None.

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