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Review Article

ECG frequency changes in potassium disorders: a narrative review

Navid Teymouri[1], Sahar Mesbah[2], Seyed Mohammad Hossein Navabian[3], Dorsa Shekouh[4], Mahsa Mohammadi Najafabadi[5], Narges Norouzkhani[6], Mohadeseh Poudineh[7], Mohammad Sadegh Qadirifard[8,9], Saba Mehrtabar[10], Niloofar Deravi[11]

[1]Student Research Committee, Tabriz University of Medical Science, Tabriz, Iran; [2]Student Research Committee, Faculty of Pharmacy, Shahid Sadoughi University of Medical Sciences, Yazd, Iran; [3]Student Research Committee, Medicine Faculty, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran; [4]Student Research Committee, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran; [5]Department of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran; [6]Department of Medical Informatics, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran; [7]School of Medicine, Zanjan University of Medical Sciences, Zanjan, Iran; [8]Department of Nursing and Midwifery, Islamic Azad University, Tehran, Iran; [9]Department of Nursing, Garmsar Branch, Islamic Azad University, Garmsar, Iran; [10]Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran; [11]Student Research Committee, School of Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran

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Abstract: Nowadays, electrocardiogram (ECG) changes are one of the valuable diagnostic clues for recognizing abnormalities. Potassium is one of the essential electrolytes in cardiac cells, and its variations affect ECG. Potassium disorders, including hyperkalemia and hypokalemia in authoritarian states, may lead to heart dysfunctions and could be life-threatening, and urgent interventions are needed in this conditions. The current review summarizes studies to elucidate the correlation between potassium disorders and ECG demonstrations. In this review, we summarized ECG changes related to hyperkalemia and interventions. Moreover; animal studies on ECG changes related to hyper- and hypokalemia are provided. The studies showed peaked T wave, as well as expanded QRS complex and low P amplitude, are important changes that can guide us to immediate diagnosis. ECG Changes in severe hyperkalemia that can endanger patients' lives are noteworthy. Manifestations change in hyperkalemia, for correct diagnosis clinical history of the patients is essential.

Keywords: ECG, potassium disorders, hypokalemia, hyperkalemia

Introduction

Myocardial cells keep up their activity of depolarization and repolarization, by developing several essential electrolytes like potassium, sodium, and calcium; their currents across the membrane can be announced by ECG [1]. Nowadays, ECG changes are one of the useful diagnostic clues for recognizing electrolyte abnormalities [2]. A significant ratio of cardiac arrests in adult patients with no coexisting cardiac disorder is due to metabolic abnormalities [3]. One essential electrolyte that impact transmembrane potential in cardiac cells is potassium concentration. The electrical stability of the heart is sensitive to potassium concentration. Its increase or reduction has profound effects on the electrophysiology of cardiac muscle [1, 4]. Membrane resting potential is related to the difference between intracellular and extracellular potassium concentrations. Therefore, increasing plasma potassium reduces this ratio, as a result, increases cell membrane excitability. In hyperkalemia conditions (potassium levels become higher than 5 mmol/L), the cardiac cells depolarise with almost no regular repolarization, which causes muscular weakness and in severe states, causes cardiac arrest in diastole [5]. In hypokalemia conditions (potassium levels become lower than 3.5 mmol/L), the cardiac cells hyperpolarise with a reduction in muscular contraction, heart rate,

and blood pressure. In authoritarian states, cardiac arrest occurs in systole [6]. Severe hyperkalemia and hypokalemia can threaten life, and immediate diagnosis and treatment are required [7]. In this review, we summarize and evaluate the studies on electrocardiogram changes following potassium disorders.

Hyperkalemia and ECG changes

According to many studies, hyperkalemia strongly correlates with ECG manifestations [8]. In this condition, as summarized by **Figure 1**, ECG changes, including expansive QRS complex, peaked T-wave, prolonged QT-interval, and hidden p-wave might be initiated [9-11]. Due to transmembrane permeability changes in high potassium levels, there are some paths to suppress this condition such as intravenous calcium chloride infusion [11] or a combination of glucose and insulin, which can transfer potassium from ECM to ICM, beta-2 adrenergic agonists, and also sodium bicarbonate [9]. Terminally in severe exceeding potassium levels, hemodialysis and sodium polystyrene sulfonate are represented as a prompt intervention [9, 11]. In severe hypokalemia (potassium level under 3 mEq/l), the U-wave might outpace the T-wave; therefore, the T-wave be masked by a giant U-wave, and the QU-interval might be considered a pseudo-prolonged QT-interval [9, 12]. Otherwise, in severe hypokalemia, ventricular tachycardia/fibrillation, atrioventricular block, and tachyarrhythmias might be seen [13]. An et al. [14] suggested risk factors, clinical demonstration, and predictors of mortality of severe hyperkalemia. They used commonly used medications for decreasing K^+ plasma levels, such as potassium-sparing diuretics, beta-blockers, angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, digoxin, non-steroidal anti-inflammatory drugs, and potassium supplements. According to their findings, 50.4% of available ECGs of patients showed changes relevant to critical hyperkalemia such as tall T waves, prolonged PR interval, shortening of QT interval, decreased P wave amplitude, sine-wave ventricular rhythms with big QRS complex, and ventricular fibrillation and asystole. Also, the duration between diagnosis to changes in ECG findings was about 22 minutes. Durfey et al. [15] declared the correlation between ECG anomaly and short-term adverse episodes in patients with hyperkalemia. They defined adverse episodes as ventricular tachycardia, symptomatic bradycardia (can be cured by calcium colored, calcium gluconate, etc.), ventricular fibrillation, cardiopulmonary resuscitation (CPR), and, or death. According to their results, in mild hyperkalemia (6.5-7 mmol/L), just 66% showed ECG abnormality, and 9% had adverse episodes. Otherwise, in severe hyperkalemia (≥ 8 mmol/L), all patients showed ECG abnormality induced by hyperkalemia, and 56% had adverse episodes. They identified prolonged QRS, junctional rhythm, and bradycardia as common ECG alterations induced by hyperkalemia with short-term adverse episodes. In conclusion, they suggested that ECG can be a predictive tool to diagnose severe hyperkalemia and recognize which hyperkalemia patients are in danger of adverse episodes. Varga et al. [16] studied hyperkalemic and normokalemic patients who had a history of CKD, heart failure, liver failure, diabetes mellitus, sepsis, cancer, hypertension, and dehydration that were more prevalent in hyperkalemic patients. Some patients in both groups received ARB, ACEI, potassium supplements, NSAIDs, β-blockers, digitalis, amiloride, and spironolactone. In their ECGs, wide QRS, peaked T waves, bradycardia, and first-degree AV block were demonstrated in both groups, AV junctional rhythm was recognized in moderate or severe hyperkalemic patients. As Varga et al. reported, ECG abnormalities associated with hyperkalemia, ST depression in both groups, atrial fibrillation, and QT prolongation more prevalent in the hyperkalemic group were demonstrated. furthermore, in comparison between severe and moderate hyperkalemia, atrial fibrillation, first-degree AV block, wide QRS, and peaked T waves were more prevalent in moderate hyperkalemic patients.

Hyperkalemia correlated with ECG can appear in metabolic disorders such as renal failure and critical illnesses, including multisystem organ failure, sepsis, and certain medications. As shown in **Figure 1**, some strong clues to hyperkalemia (potassium level at least 8.2 mmol/L) in patients suffering from renal failure, might be present as the narrow QRS complex, sinus rhythm, and peaked T-wave, which are more slight than manifestations of potassium level at about 6.3 mM/L as there is ST-elevation, and the QRS-complex widening [17]. Even though these peaked and high amplitude T-waves

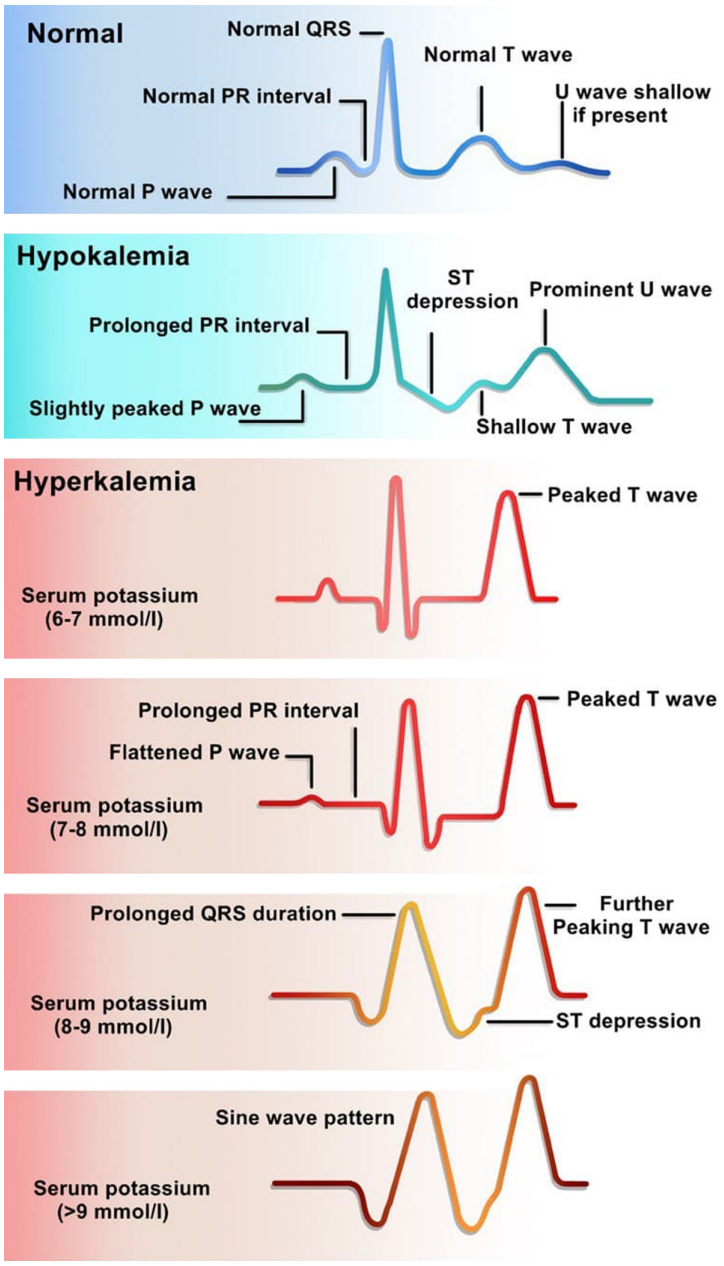

Figure 1. Hyperkalemia, hypokalemia, and ECG changes. Progressive hyperkalemia may result in ECG changes, including peaked T wave, flattened P wave, prolonged PR interval, ST depression, and prolonged QRS duration. Besides, hypokalemia may associate with a peaked P wave, prolonged PR interval, prominent U wave, shallow T wave, and ST depression.

could consider the most prompt manifestation of hyperkalemia [18], these T-waves, with no other signs, are hardly the clue for the lethal condition [17]. Otherwise, in severe conditions of high levels of potassium, T-wave and QRS complex fusing might be present. Furthermore, in severe conditions, the velocity of the his-Purkinje system is reduced and might be terminated to bundle brunch block and fascicular blocks [18]. Therefore, in the patients with absence of P-wave, widening and the abnormal axis of QRS-complex, sine waves, sinus bradycardia or sinus arrest, with ventricular pre-excitation loss in patients suffering from Wolff-Parkinson-White syndrome, double counting of the heart rate according to masked T-waves, and even though, pulseless electrical activity, subsequently, and electrocardiographic STEMI or Brugada pattern or in some conditions, Dressler-de Winter mimicry, might be reflected as constant signs of a life-threatening condition [17]. Madias et al. [19] proved that ST-segment elevation is the result of hyperkalemia pseudo-infarctional ECG manifestation, in which the intracellular/extracellular potassium ratio is considered the cause of these illusory changes, however, a rise terminated in ST-segment depression, and a reduction resulted in ST-segment elevation. Several studies showed that tall "peaked" T waves are the common symptoms of severe hyperkalemia [20-22]. Also, Fordjour et al. [20] reported that patients with obvious peaked T wave received more calcium intervention than other no ECG-changed patients which suggested that physicians used ECG as a marker for calcium administration in patients with hyperkalemia. However, some studies proved that T waves alterations of ECG are not valid predictors for serum potassium concentration and hyperkalemia episodes and should not be counted on in patients in the emergency department [21, 23]. Wong et al. [24] reported an ECG of a patient with "peaked" T waves, P waves absence, slight R wave progression, and QRS interval flatting. The level of serum potassium was 10.4 mmol/ml. An ampule of D50, Calcium gluconate, sodium

bicarbonate, and also 10 units of insulin were injected intravenously with oral Kayexalate. In the repeated ECG, returning of P waves, QRS interval narrowing, improvement of the R wave, and for the T wave less peaking was demonstrated when the level of the potassium was 9.2 mmol/L. Despite medical therapy for lowering potassium levels, returning of the peaked T wave, PR interval prolongation, and widening of QRS interval to 205 msec were shown in 3th ECG though the level of the potassium was 10.0 mmol/L. After dialyzing, they reported that the level of the potassium became normal and returned to the baseline ECG. Chronic renal dysfunction may correlate with the toxic effect of hyperkalemia and morphology changes on ECG [25, 26]. Khattak et al. [27] reported an 84-year-old female who had normal kidney function, with clinical signs of dehydration, previously diagnosed with hypertension, pulmonary hypertension, chronic heart failure, cerebrovascular accident, and multiple nodules in the liver and lungs with potassium levels at about 10.1 mEq/l and used some medications include lovastatin, Lasix, Felodipine, aspirin, Atrovent, and albuterol inhalers. Her ECG revealed left ventricular hypertrophy with normal sinus rhythm (80 beats per minute), normal QRS complex, and PR interval, although the T-waves were inverted. After hyperkalemia correction the ECG normalized, and T-waves became normal. This hyperkalemic condition occurred twice for her, and there was another T-waves inversion without any usual signs of hyperkalemia; despite her high potassium level (8.5 mEq/L). After that, some tests revealed hypoaldosteronism with metastatic adenocarcinoma of the lung. Consequently, hyperkalemia suppress action potential conduction between myocytes [9]. Therefore, some ECG manifestations occur, including PR interval prolongation, QRS duration increasing, T waves sharpening, and ventricular fibrillation. These ECG changes normally occur by moderate changes in potassium level (6.5-7.6 mEq/L), but in severe changes, mostly there are some classic ECG manifestations [25]. Esposito et al. [25] reported that left ventricular hypertrophy, intraventricular condition, and myocardial ischemia might camouflage ECG changes in exceeding potassium levels. Kuvin et al. [28] reported a 42-year-old female suffering from end-stage renal dysfunction and underwent an arteriovenous anastomosis as permanent hemodialysis. As she went under this surgery, her electrocardiogram manifested a complete heart block in addition to ventricular escape. Afterwards, twice injections of calcium made her ECG quite abnormal, which demonstrated left-bundle-branch-block (prolonged QRS complex), first-degree atrioventricular block, sinus tachycardia, and peaked T-waves. Her serum potassium level was 8.6 mmol/L; Thereupon, after hyperkalemia correction, the sinus rhythm and other ECG manifestations were normalized. Kurisu et al. [29] reported an 89-year-old man who was referred to the clinic with the signs of hyperkalemia; junctional bradycardia, saddle-back, and coved ST-segment elevation. By following, the Brugada-like electrocardiogram was initiated to normalize, as the serum potassium decreased at about 5.4 mEq/l. Ryuge et al. [30] described a warning of the normality of ECG in a patient with severe hyperkalemia. A 77-year man with chronic renal failure, severe hyperkalemia (K^+, 8.5 mmol/L), and normal ECG was admitted. His hyperkalemia was due to gastric cancer, and its intervention includes carvedilol, enalapril, and spironolactone. Instead of chemotherapy. In contrast, his general condition got worse, and sine-wave ventricular tachycardia was seen in his ECG, so previous treatment returned. This case declared that sometimes ECG alterations are not caused by the level of hyperkalemia; they may be established by the development of hyperkalemia.

Hyperkalemia is a usual problem in patients with CKD, HF, and diabetes mellitus [31]. According to Rafique et al. [32], there were 66 patients with ESRD and 38 of them were men with 45.8 mean age, 39 of them had hyperkalemia, and 20 of them had potassium levels in the range of tough hyperkalemia. Of the 5028 ECGs given to these ESRD patients, the currency of Hyperkalemia was 60%, and minimally 50% of them were in the challenging hyperkalemia range. Changes in ECGs were not significant; for example, raised QRS length was 14% and 6% prolonged PR duration in cases had hyperkalemia. This cohort study showed that ECG is not a sensitive method, but it has high specificity.

Hyperkalemia and ECG changes and their diagnosis, treatment, and related medication

Diagnosis of hyperkalemia was performed by Chon et al. [33]. This study showed how to diag-

nose severe hyperkalemia in patients according to their history, quantitative ECG findings, and vital signs. Their research contained patients at the emergency department who have extreme bradycardia (heart rate [HR] ≤40/min) or symptomatic bradycardia (HR ≤50/min with chest pain, dyspnea, altered mentality, general weakness, syncope, oliguria, or shock) for the duration of 46 months. In this study, 21.3% of these cases had critical hyperkalemia. Therefore, extreme or symptomatic bradycardia is not a risk factor, but can be clinical evidence for severe hyperkalemia. The diagnostic risk factors of hyperkalemia are junctional bradycardia (JB) or atrial fibrillation (AF) (score 1), heart rate lower than 42/min (score 1), maximum precordial T-wave more than 8.5 mV (score 2), diltiazem medication (score 2), and diabetes mellitus (score 1). If in a case, the total score is four or higher with a positive likelihood of 6.02, the sensitivity of 0.50, and specificity of 0.92, severe hyperkalemia may be diagnosed. If we check this by ECG-only index (maximum precordial T-wave more than 8.5 mV, heart rate lower than 42/min, and JB/AF), the score of 3 or higher may detect severe hyperkalemia with a positive likelihood of 5.10, the sensitivity of 0.50, and specificity of 0.90.

9% of patients suffering from chronic kidney disease (CKD) spent some time with hyperkalemia (5.5 mEq/L or more) [34]. Galloway et al. [35] appraised the performance of a deep-learning model to detect hyperkalemia which can lead to fatal arrhythmias from ECG in patients suffering from CKD. ECG showed changes in T-wave and QRS structure associated with a high potassium level. In Wrenn et al. [36] study, the patients were diagnosed with renal insufficiency and hyperkalemia. Increased T-wave amplitude, absence of P-waves, prolonged, decreased P-wave amplitude, and sinusoidal QRS-T appearance is considered hyperkalemic ECG criteria. They indicated hyperkalemia as a cause of decreasing resting membrane potential and QRS prolongation. They also considered that the increasing velocity of the third phase of action potential was due to the increased potassium permeability and therefore, the shortening of QT-interval and peaked T-waves [37-40]. In severe cases, ventricular tachycardia or fibrillation [39], bifascicular block, right or left bundle-branch blocks [41], complete heart block [42], or acute myocardial infarction might occur under hyperkalemic status [43]. Ventricular diastolic overload, subendocardial ischemia, bradycardia, hyperacute T-waves, and cerebrovascular accident may mimic hyperkalemic manifestations [36]. Moreover, the rate of progression of hyperkalemia may affect the ECG manifestations, in which a rapid increase of serum potassium may affect heart rate primarily than the other signs [44, 45]. Patients receiving frequent hemodialysis are more in danger of developing heart diseases and arrhythmias than other people [46]. Most heart diseases are due to intracellular and extracellular potassium concentration [47]. QT interval was associated with the increased risk of arrhythmia. This study designed by Buemi et al. [48] demonstrated the impacts of two significant methods of potassium removal through hemodialysis on ECG patterns. It was found that the QT interval had a significant reduction in variable potassium concentration (VPC) vs constant potassium concentration (CPC). In conclusion, hemodiafiltration with variable potassium concentration removal causes a lower risk of arrhythmia rather than constant potassium concentration. In fact, with CPC hemodiafiltration, the cardiac cell membrane hyperpolarizes more which has a destabilizing effect and causes backward circuits.

To determine symptoms of hyperkalemia, Littmann et al. [49] have provided an ECG interpretation software that can readily show signs of high serum potassium level. In this study, 33 patients with double-counted heart rates were diagnosed with hyperkalemia. In 18 cases, serum potassium level was about 7.0 mEq/l or higher. Some patients were diagnosed with renal insufficiency, diabetic ketoacidosis, alcoholic ketoacidosis, severe respiratory acidosis, and some others with multisystem organ failure and sepsis. Although nine patients had a narrow QRS appearance, the rest had widened QRS complex. Furthermore, in 4 cases, paced rhythm or left bundle-branch block emerged. In 3 patients, sine-wave appeared. Duo to double-counted heart rate, which does not appear in normokalemic status, it was considered that where there were not any noticeable signs of high-level serum potassium, there were symptoms of hyperkalemia.

In one important study, Corsi et al. [50] established a method to quantify potassium concentration from ECG analysis in two patients with

frequent hemodialysis (significantly variable potassium levels) and long QT syndrome type 2. They analyzed T waves of QRS, especially downslope/amplitude of T waves and checked the relationship between $T_{S/A}$ and serum potassium levels. It was found that in dialysis patients, a significant T waves alteration morphology was observed, and that was due to the injection of potassium. As a result, $T_{S/A}$ had a meaningful relationship with potassium concentration. They discovered a computational relation "$K_{ECG} = 0.36 \times T_{S/A}^2 + 0.22 \times T_{S/A} + PB$" ($K_{ECG}$: potassium concentration estimated by ECG analysis; PB: patient-specific bias, 1.96 ± 0.85 mM) for ECG-based K^+ evaluator which was corrected for patient-specific bias. This equation was confirmed by Leave-one-out cross-validation and the average error of estimated [K^+] (K_{ECG}) was -0/09 ± 0.59 mM and the average absolute error was 0.46 ± 0.39 mM.

Hyperkalemia can lead to death if not diagnosed. In studies done by Siddiqui et al. [51], three death cases related to Hyperkalemia in HD patients (with a serum potassium of 7.4 to 8.0) were reported. As there were no apparent signs of hyperkalemia ECG among HD patients, it was difficult for the doctors to diagnose the symptoms. As a result, the potential life-threatening hyperkalemia was raised. Aslam et al. [52] announced that there were no particular ECG symptoms related to hyperkalemia in HD patients; nevertheless, in that inquiry, the researchers had only evaluated the T wave magnitude as well as T wave to R wave magnitudes ratio and their correlation with Calcium concentration and serum potassium. Eghlim et al. [53] performed a study of 36 females and 44 males with terminal-stage renal disease. Analysis revealed a critical inverse association between potassium of serum and T wave duration. In Patients with a level of potassium in serum more than 5.6 mg/dl, T wave duration was no more than 200 ms. It also was revealed that there is a critical relationship between Hyperkalemia and reduced T wave duration.

Martinez-Vea et al. [26] showed that treatment with glucose, Salbutamol, NaHCo3, and insulin reduces potassium concertation. In a study done by Petrov et al. [54], a 62-year-old man was reported. The man was suffering from chronic renal failure and had decreased exercise tolerance one week before he went to the hospital. An ECG revealed an expanded QRS compound, PR prolongation, and there were no detectable P waves. The potassium level of the patient's serum was 9.1 mmol per liter which raised doubt of severe hyperkalemia. After a wide range of treatments such as controlling the high level of blood sugar, bicarbonate, and using insulin therapy as well as calcium chloride (which was caused by hemodialysis) his situation was stabilized. Serial ECG revealed developmental narrowing of the QRS compound. On the fowling day after the treatment, ECG showed a pattern of a left bundle-branch and his situation remained stable.

The similarity of ECG changes caused by hyperkalemia and other diseases

It has been reported in a large number of cases that moderate to severe Hyperkalemia can influence or change electrocardiogram [43, 55, 56]. In one of the case studies published by Chawla et al. [57], it was discussed that electrocardiogram changes of acute myocardial infarction sometimes have similarities with hyperkalemia which may cause inappropriate diagnosis. In their study, a 48-year-old man who had been suffering from diabetes was controlled with NPH insulin. His examination showed hyperkalemia, acidosis, and ketonemia which were serious symptoms of diabetic ketoacidosis. His ECG showed, however, the elevation of ST-segment, acute anterior wall injury, and also tall peaked T waves which were symptoms of hyperkalemia. For closed monitoring and acute diabetes ketoacidosis treatment contains sodium bicarbonate, fluid replacement, and regular insulin. His blood sugar and serum K^+ decreased while pH and S. His serum bicarbonate level increased after treatment. Furthermore, ECG showed a reduction of ST-segment elevation, and T wave tending persisted. Finally, in the last examination, all parameters appeared to be normal. They demonstrated treatment of hyperkalemia in patients who have diabetes ketoacidosis and hyperkalemia with an ECG simulating an acute anterior wall myocardial infarction causes an immediate return of the ECG to normal. A 20-year-old male patient with type 1 diabetes was revised by Sims et al. [58]. He was diagnosed with nausea, vomiting, and abdominal pain which lasted for about 8 hours. From his blood test, they diagnosed diabetic ketoacidosis (DKA). The patient's potassium concentration was 9.4 mmol/L and his ECG findings showed: ST-seg-

ment elevation, absent P waves, wide QRS complex with bradycardia, peaked T waves in leads of V_1, V_2, and aVR. With the medication of calcium gluconate, bicarbonate, and insulin his ECG changes were coming back to normal due to the reduction of serum potassium levels. Hardly, the elevation of ST-segment is associated with myocardial infarction which in this study it was defined as a pseudo-infarction pattern. A case of hyperkalemia and pseudo myocardial infarction was reported by Simon et al. [59]. A 59-year-old man with acute anterior myocardial infarction was presented. The patient was on medication such as insulin infusion, calcium gluconate, and sodium bicarbonate for lessening the potassium levels. After two hours of examination, the patient serum potassium level was 5.4 mmol/L and ECG abnormalities were lost. There were some clues of hyperkalemia in this case, but symptoms of myocardial infarction were more obvious, and if these symptoms are not diagnosed, there won't be an effective treatment, and as a result, patients will be in danger of severe heart diseases.

Brugada syndrome is a new electrocardiographic syndrome with irregularity of sodium channel, which usually causes sudden cardiac death in patients without structural heart disease [60, 61]. Reingardienė et al. [62] discussed some cases with Brugada-like ECG patterns caused by hyperkalemia. A renal failure with hyperkalemia was the cause of Brugada-ECG in all the patients. By returning serum potassium levels to the normal values in all the patients, ECG changes disappeared. The range of potassium levels from 6.0 to 8.8 mmol/L induces hyperkalemia Brugada ECG patterns. Additionally, when ECG alterations are seen, drugs that block cardiac sodium channels should not be used to decrease the probability of arrhythmias. The Brugada electrocardiographic manifestation may be an ephemeral sign of non-genetic disease [63-65]. However, the usual correlation with the Brugada ECG pattern might be right ventricular pathology. A few cases of hyperkalemia-induced Brugada ECG pattern were reported [63-69]. Furthermore, cardiac sodium channel abnormalities are considered to cause Brugada syndrome [70]. Several studies showed that the Brugada ECG pattern followed by axis shift, absence of P-waves, ST-segment elevation accompanied by negative T-waves, and widened QRS complex might be considered as a notice for fatal hyperkalemia [70, 71]. Moreover, some studies reported pseudoinfarction pattern as an ECG manifestation in hyperkalemic status [19, 58, 59, 72, 73]. In a study done by Postema et al. [74], a patient and his 30-year-old son who had no medical history were reported. Their test provoked Brugada type 1 ECG features. The study illustrated that hyperkalemia and acidosis can bring about Brugada syndrome. In a study reported by Omar et al. [75], a 31-year-old man who had type 1 diabetes mellitus continued hospitalization because of diabetic ketoacidosis (DKA). The patient also used intravenous drugs. Laboratory workup showed a potassium level of 8.4 meq/l. It was also reported that ECG revealed hyperacute T waves as well as Brugada type 1 with increased duration of QRS correlated with ST-segment high take-off in V_1-V_2 chased by down-slanting ST-segment and proportion T waves inversion. After nine hours of suitable treatment for DKA, potassium was 3.8 meq/l and ECG revealed resolve of ST-segment elevation.

Hyperkalemia and its related ECG changes in other disease medications and operations

In older patients, the most common reason for hyperkalemia is due to the application of iatrogenic medication associated with the etiology of other diseases which can decrease normal metabolic capacity [76]. Here; Berkova et al. [77] reported two cases of old patients with severe hyperkalemia. The first case was an 83-year-old woman referred to ED for the generalized weakness of muscle and bradycardia (40/min). Mitral valve deficiency, arterial hypertension, type 2 diabetes managed by diet therapy, nephropathy with proteinuria, and having proximal atrial fibrillation were in her medical history (then she was treated with losartan, digoxin, diltiazem, warfarin 3, spironolactone, and amiloride-hydrochlorothiazide). Her potassium level was 9.62 mmol/L, and according to her ECG, they observed no atrial electric activity, abnormal QRS complex, and picked T waves. She received calcium gluconic, glucose/insulin, rehydration infusions, sodium bicarbonate, Furosemide, and Calcium meconium (for fortifications treatment). With this medication, her PQ interval was prolonged, her QRS complex

was narrowed, and her heart rate became 70/min. After her serum potassium level returned to normal, her muscle weakness lessened. The second case was a 73-year-old man referred to the hospital for progressing lower muscle weakness. He had a history of hypertension, type 2 diabetes managed by insulin therapy, myocardial infarction, chronic atrioventricular block, and coronary artery bypass grafting (his medication included ramipril, chronic intensive insulin therapy, amiloride-hydrochlorothiazide, spironolactone, acetylsalicylic acid, and rosuvastatin). His serum potassium level was 9.0 mmol/L, and ECG findings showed strange wide QRS and undifferentiated P waves with a heart rate of 73/min. For urgent medication, he was given a sodium chloride solution, Humulin, sodium bicarbonate, Calcium gluconic, Furosemide, and Calcium meconium. After remission of serum biochemistry values, bizarre ECG was lost, and a sinus rhythm with narrowed QRS and the first-degree chronic atrioventricular block was seen. They concluded that while potassium-sparing drugs can cause developmental hyperkalemia, physicians should frequently monitor serum K^+ levels in patients using these drugs. The patients who need pacemaker implantation due to rhythm anomaly, are more susceptible to hyperkalemia because of pharmacological treatment [78]. Bahl et al. [79] reported a case where common ECG changes due to hyperkalemia were observed during pace rhythms. In this study, a 56-year-old woman with a constant pacemaker because of a complete heart block presented with syncope. She had mild mitral regulation and severe left ventricular systolic abnormality. They discharged her on amiodarone, carvedilol, ramipril, warfarin, frusemide, and spironolactone. ECG findings demonstrated an expansive QRS complex merged with T wave, no significant P waves, and all beets were paced. Serum K^+ level was 6.0 mmol/L. She also had calcium gluconate, glucose-insulin infusion, and potassium binding resin for getting management. After treatment, her ECG showed paced-beets again, but QRS was narrowed and had sharper peak and P waves were apparent in leads of V_1 and V_2. Because of decreasing in 0 phrases of the action potential, QRS becomes wider and T wave blends to QRS complex and it can be easily seen even in this case. So, analyzing ECG still is useful diagnosing hyperkalemia even in the patient using a pacemaker. In another study, Suzuki et al. [80] reported an experience of ECG deficiency with hyperkalemia within the operation. A 65-year-old man who had diabetes and hypertension for many years (taking hypoglycemic and hypertensive drugs like an angiotensin-converting enzyme (ACE) and angiotensin receptor blockers (ARB)) underwent an operation for a maxillary sinus cyst. Within the operation, they detected unexpected ECG alterations, including widened QRS complex and peaked T waves. By checking serum potassium, they found these changes were caused by hyperkalemia. They gave the patient saline infusion, Furosemide and calcium gluconate injection, and glucose-insulin therapy which resulted in normal ECG and other clinical parameters. They discussed diabetes and the application of ACE and ARB might have induced hyperkalemia.

Animal studies on ECG changes related to hyper- and hypokalemia

Several animal studies have proved ECG changes related to hyper- and hypokalemia. In one study, Akita et al. [81] checked ECG changes in hypokalemia induced by Furosemide in the rats. In rats, the T wave is placed immediately after the complex of QRS; hence no significant ST segment can be identified. Despite human studies, T wave changes were not observed in rats. According to their results, P wave and QRS complex were prolonged obviously, but PR interval change was less significant. This suggests that extracellular potassium level influences myocardium excitabilities in the ventricles and atria rather than influenced by the atrioventricular conduction system. In contrast to humans and dugs, U wave cannot be seen in rats in hypokalemia cases. Tag et al. [82] divided 37 cats and dogs into five groups according to the level of their serum potassium. They had a history of obstruction of urethral, renal disorders, hypoadrenocorticism, pseudo-hypoadrenocorticism, tumor lysis syndrome (acute), over-supplementation, diabetes mellitus, pancreatitis, and diabetic ketoacidosis as the result of hyperkalemia. In the first group (5.5-6.49 mEq/L), ECGs showed normal sinus rhythm and forms and sinus bradycardia and sinoventricular rhythm. The second group (6.6-6.99 mEq/L) had ECGs with normal sinus rhythm. The third group (7.0-8.49 mEq/L) had normal sinus rhythm, but sinus tachycardia

and tall T waves were demonstrated. ECGs of the fourth group (8.5-9.99 mEq/L) were normal in sinus rhythm, while ventricular tachycardia was shown in a cat with a urethral obstruction. Tall T waves, bradycardia, and standstill of atrial were demonstrated. Sinus tachycardia and normal sinus rhythm were demonstrated in ECGs of the fifth group (equal or more than 10 mEq/L), at same time, in a dog with hypoadrenocorticism, a second-degree block of atrioventricular was also found. Laboratory data showed abnormalities such as hyponatremia (49%), hypermagnesemia (67%), hypochloremia (43%), hypermagnesemia (67%), hypocalcemia (20%), and venous acidemia (94%). Linear regression showed no important relationship between potassium level and heart rate in cats and dogs, except in cats with a serum potassium of more than 8.5 mEq/L. Hiatt et al. [83] designed a study on four mongrel dogs to determine the changes in ECG affiliated with hyperkalemia. The dogs were infused with potassium in different amounts, and the electrocardiogram changed in different manifestations as in the potassium excess by almost 50% the PR-interval prolonged, and P-wave and AV nodal activity initiated to disappear (at about 7 mmol/l), at following by more accretion of the potassium level (at about 8 mmol/l), ventricular pacemakers set up the cardiac rhythm and ventricular fibrillation appeared. They mentioned that the cardiac response to serum potassium excess under such conditions, likewise potassium increasing due to soft tissue trauma is an efficient response for hyperkalemia. In another study designed by Hiatt et al. [84], kaliuresis is considered a regulating mechanism for serum potassium which can be either ensuing by kaliuresis independent pathway by transferring the extra potassium from extracellular fluid to intracellular fluid as well in cardiac cells happen and made these changes to ECG afterwards. Kuwahara et al. [85] presented a study confirming the association between potassium levels and ECG abnormalities. They divided 61 rats into three groups. Group A and B were nephrectomized and infused with fluid that did not have any electrolytes, including potassium, but group C imbued high-potassium-containing fluid. They determined that the first sign of potassium increase is sharping, narrowing, increasing the amplitude of T-waves, and hiding ST-segment in some ECGs. In moderate to severe hyperkalemia, QRS and P waves duration were increased, P wave amplitude significantly decreased, and PR and QT intervals were prolonged (although in moderate hyperkalemia, PR interval could slightly decrease). Moreover, heart rate was notably decreased in severe hyperkalemia, and also in the most severe increasing potassium level, a sine wave ECG could be seen [56]. In another study reported by Cohen et al. [86] provided that, according to the results, the effect of hyperkalemia on His Purkinje is much slower than those in the conduction system. In the study designed by Hiatt et al. [87], 21 dogs were divided into three groups; in group A the dogs were adrenalectomized, group B was phonily adrenalectomized for almost an hour, and group C did not go under any procedure. The ECG manifestation emerged in adrenalectomized dogs at serum K level 4.5 mEq/l; however, the fatal ECG manifestations such as the widening of QRS complex, T-wave and p-wave changes, nodal and ventricular rhythm appeared at potassium level nearby 7.95 mEq/l while it initiated to appear at about 9.68 Eq/L potassium level in group B and about 10.17 mEq/l in group C. Other studies proved that K ion infusion in adrenalectomized animals caused greater toxicity than normal animals [88, 89]. Even though in previous studies, death was the endpoint of the fatal potassium level, in this study, the termination of ECG changes was not death. Another study in rats demonstrated that chronic deficiency of adrenal hormones might influence the permeability of myocardial cells in which there was a 15-25% reduction in myocardial permeability in a condition that serum potassium concentration was elevated, in contrast the ICF potassium in cardiac cells was decreased [90]. Porter et al. [91] reported ten dogs that underwent special protocol three times. 2 meq/kg/hr of KCl was given IV till p waves were stayed away from the ECG, under isoflurane anesthesia, and ventricular rates reduced more than 20% in less than 5 minutes. A three-layer synthetic neural system with four latent nodes was trained, and its purpose was to foretell potassium from 15 separate components of harmonizing ECG data. Data were separated into test sets and training sets. ANN or artificial neural network was considered to foretell hyperkalemia from information accommodated in the standard appearance of ECG.

Conclusions and future perspectives

The sensitivity of ECG changes for the diagnosis of mild hyperkalemia is poor, but an increased potassium level can positively affect it. Peaked T wave, expanded QRS complex, and Low P amplitude, are essential changes that can guide us to immediate diagnosis. ECG Changes in severe hyperkalemia that can endanger patients' lives are noteworthy. These changes in the elderly, which can be along with a history of renal failure or diabetes, are signs that should be considered.

Progressive hyperkalemia may result in ECG changes, including peaked T wave, flattened P wave, prolonged PR interval, ST depression, and prolonged QRS duration. Besides, hypokalemia may associate with a peaked P wave, prolonged PR interval, prominent U wave, shallow T wave, and ST depression. Changes in serum potassium concentrations may cause life-threatening arrhythmias. The importance of early diagnosis and approach to hyperkalemia is important for physicians due to its hazards. We found that although ECG changes like peaked T waves, expanded QRS complex, or low amplitude P waves were corroborative tests for hyperkalemia, but ECG alone had minimal value to diagnosis; because we could not trust it to rule out hyperkalemia, and it must use with clinical history.

Disclosure of conflict of interest

None.

Address correspondence to: Mohammad Sadegh Qadirifard, Department of Nursing, Garmsar Branch, Islamic Azad University, Daneshgah Street, Garmsar 35816-31167, Iran. Tel: +989300848749; E-mail: ms.qadirifard@gmail.com; Niloofar Deravi, Student Research Committee, School of Medicine, Shahid Beheshti University of Medical Sciences, Arabi Ave, Daneshjoo Blvd, Velenjak, Tehran 19839-63113, Iran. Tel: +989193195717; E-mail: niloofarderavi@sbmu.ac.ir

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