



Article

Hyperkalemia Risk After Finerenone Initiation in Diabetic Kidney Disease with Elevated Baseline Potassium: A Multicenter Cohort Study

Alper Tuna Güven ^{1,*}, Serap Yadigar ², Murat Özdede ³, Suat Akgür ⁴, Felemez Arslan ⁵, Mehmet Sezen ⁶, Büşra Özcan ⁷, Elif Yıldırım Ayaz ⁸, Betül Doğanekin ⁸, İlker Atay ⁹, Serpil Müge Değer ⁹, Mustafa Demir ¹⁰, Sümeysa Koyuncu ¹⁰, Üstün Yılmaz ¹¹, Ayça İnci ¹², Hülya Çolak ¹³, Bülent Demirelli ¹⁴, Serhan Tuğlular ¹⁵, Ebru Gök Oguz ¹⁶, Mehmet Deniz Ayli ¹⁶, Ezgi Avanaz ¹⁷, Fatih Yılmaz ¹⁸, Beyza Doğan ¹⁹, Süleyman Karaköse ¹⁹, Mine Şebnem Karakan ²⁰, Bahar Gürlek Demirci ²⁰, Kültigin Türkmen ²¹, İsmail Baloğlu ²¹, Mehmet Batmazoğlu ²², Mehmet Mert ²³, Emre Aydın ²⁴, Fatma Yılmaz Aydın ²⁵, Ergün Parmaksız ², Pınar Özdemir ², Bartu Ediz ², Zeki Aydın ²⁶, Mehmet Emin Demir ²⁷, Siren Sezer ²⁷, Suat Ünver ²⁸, Öznur Baykal ²⁹, Beril Akman ³⁰, Atila Altuntaş ³¹, Mahmud İslam ³², Sibel Yücel Koçak ³³, Meral Mert ³⁴, Belda Dursun ³⁵, Necmi Eren ³⁶, Simge Bardak Demir ³⁷, Mukadder Ayşe Bilgiç ³⁸, Arda Erdut ³⁹, Gülşah Keskin ⁴⁰, Mehmet Horoz ⁴¹, Ahmet Ziya Şahin ⁴², Merve Tekinyıldız ⁴³, Murat Duranay ⁴³, Serkan Feyyaz Yalın ², Hazal Melike Yavuz Umut ², Murat Altunok ⁴⁴, Ramazan Sarı ⁴⁵, Funda Sarı ⁴⁶, Dilek Torun ⁴⁷, Serdar Kahvecioğlu ⁴⁸, Asena Serap Karatutlu ⁴⁹, Tülin Akagün ⁵⁰, Hüseyin Çelik ⁵¹, Sinan Kazan ⁵², İlyas Öztürk ⁵³, Mehmet Polat ⁵⁴, Mehmet Fethullah Aydın ⁵⁵, Meral Meşe ², Asil Demirezen ⁵⁶, Ülver Derici ⁵⁶, Eda Altun ⁵⁷, Serkan Bakırdöğen ⁵⁸, Ekrem Kara ⁵⁹, Cüneyt Akgöl ⁶⁰, Mahmut Başar Aykent ⁶¹, Ali İlter ⁶², Ahmet Ekmekci ⁶³, Sena Ulu ⁶⁴, Mustafa Arıcı ³⁹, Erkan Şengül ⁶⁵ and Elif Arı Bakır ⁶⁶

- ¹ Division of General Internal Medicine, Department of Internal Medicine, Faculty of Medicine, Marmara University, 34854 İstanbul, Türkiye
- ² Department of Nephrology, Kartal Dr Lütfi Kırdar City Hospital, 34865 İstanbul, Türkiye
- ³ Division of General Internal Medicine, Department of Internal Medicine, Faculty of Medicine, Hacettepe University, 06100 Ankara, Türkiye
- ⁴ Nephrology Clinic, Bursa Çekirge State Hospital, 16090 Bursa, Türkiye
- ⁵ Clinic of Internal Medicine, Bakırköy Dr. Sadi Konuk Training and Research Hospital, Health Sciences University, 34147 İstanbul, Türkiye
- ⁶ Department of Nephrology, Bursa City Hospital, 16110 Bursa, Türkiye
- ⁷ Division of Endocrinology and Metabolism, Atatürk Sanatoryum Training and Research Hospital, 06290 Ankara, Türkiye
- ⁸ Department of Internal Medicine, Sultan 2. Abdülhamid Han Training and Research Hospital, Health Sciences University, 34668 İstanbul, Türkiye
- ⁹ Division of Nephrology, Department of Internal Medicine, Faculty of Medicine, Dokuz Eylül University, 35210 İzmir, Türkiye
- ¹⁰ Nephrology Clinic, Kayseri City Hospital, Health Sciences University, 38080 Kayseri, Türkiye
- ¹¹ Nephrology Clinic, Antalya Training and Research Hospital, Health Sciences University, 07100 Antalya, Türkiye
- ¹² Division of Nephrology, Department of Internal Medicine, Faculty of Medicine, Akdeniz University, 07070 Antalya, Türkiye
- ¹³ Nephrology Clinic, İzmir City Hospital, Health Sciences University, 35540 İzmir, Türkiye
- ¹⁴ Nephrology Clinic, Marmara University Hospital, 34899 İstanbul, Türkiye
- ¹⁵ Division of Nephrology, Department of Internal Medicine, Faculty of Medicine, Marmara University, 34722 İstanbul, Türkiye
- ¹⁶ Department of Nephrology, Etlik City Hospital, Health Sciences University, 06170 Ankara, Türkiye
- ¹⁷ Nephrology Clinic, Antalya City Hospital, 07080 Antalya, Türkiye
- ¹⁸ Nephrology Clinic, Antalya City Hospital, Health Sciences University, 07080 Antalya, Türkiye
- ¹⁹ Nephrology Clinic, Konya City Hospital, Health Sciences University, 42020 Konya, Türkiye
- ²⁰ Division of Nephrology, Department of Internal Medicine, Ankara Yıldırım Beyazıt University, 06760 Ankara, Türkiye
- ²¹ Division of Nephrology, Department of Internal Medicine, Faculty of Medicine, Necmettin Erbakan University, 42090 Konya, Türkiye



Academic Editors: Antonios H. Tzamaloukas and Lucio Manenti

Received: 16 June 2026

Revised: 16 July 2026

Accepted: 21 July 2026

Published: 23 July 2026

Copyright: © 2026 by the authors.

Licensee MDPI, Basel, Switzerland.

This article is an open access article distributed under the terms and conditions of the [Creative Commons Attribution \(CC BY\)](https://creativecommons.org/licenses/by/4.0/) license.

- 22 Nephrology Clinic, Denizli State Hospital, 20010 Denizli, Türkiye
- 23 Nephrology Clinic, Özel Sağlık Hospital, 20040 Denizli, Türkiye
- 24 Division of Nephrology, Department of Internal Medicine, Faculty of Medicine, Dicle University, 21280 Diyarbakır, Türkiye
- 25 Department of Internal Medicine, Faculty of Medicine, Dicle University, 21280 Diyarbakır, Türkiye
- 26 Department of Nephrology, Darıca Farabi Training and Research Hospital, Health Sciences University, 41700 Kocaeli, Türkiye
- 27 Internal Medicine and Organ Transplantation, Department of Nephrology, Medicana International Ankara Hospital, School of Medicine, Atılım University, 06830 Ankara, Türkiye
- 28 Department of Internal Medicine and Nephrology, Acıbadem Hospital, 34758 İstanbul, Türkiye
- 29 Department of Nephrology, Basaksehir Cam and Sakura City Hospital, 34480 İstanbul, Türkiye
- 30 Department of Internal Medicine and Nephrology, Acıbadem Hospital, 34758 Ankara, Turkey
- 31 Division of Nephrology, Department of Internal Medicine, Faculty of Medicine, Suleyman Demirel University, 32260 Isparta, Türkiye
- 32 Department of Nephrology, Faculty of Medicine, Sakarya University, 54050 Sakarya, Türkiye
- 33 Department of Nephrology, Bakırköy Dr. Sadi Konuk Training and Research Hospital, Health Sciences University, 34147 İstanbul, Türkiye
- 34 Endocrinology Clinic, Bakırköy Dr. Sadi Konuk Training and Research Hospital, Health Sciences University, 34147 İstanbul, Türkiye
- 35 Department of Nephrology, Faculty of Medicine, Pamukkale University, 20160 Denizli, Türkiye
- 36 Department of Nephrology, Faculty of Medicine, Kocaeli University, 41001 Kocaeli, Türkiye
- 37 Department of Nephrology, Yenimahalle Education and Research Hospital, Ankara Yıldırım Beyazıt University, 06760 Ankara, Türkiye
- 38 Department of Nephrology, Ankara Medical Park Hospital, 06120 Ankara, Türkiye
- 39 Division of Nephrology, Department of Internal Medicine, Faculty of Medicine, Hacettepe University, 06100 Ankara, Türkiye
- 40 Division of Endocrinology and Metabolism, Haydarpaşa Numune Training and Research Hospital, Health Sciences University, 34668 İstanbul, Türkiye
- 41 Department of Nephrology, Faculty of Medicine, Health Sciences University Adana, 01370 Adana, Türkiye
- 42 Department of Nephrology, Adana City Hospital, Health Sciences University, 01370 Adana, Türkiye
- 43 Division of Nephrology, Department of Internal Medicine, Ankara Training and Research Hospital, 06230 Ankara, Türkiye
- 44 Department of Nephrology, Trabzon Kanuni Training and Research Hospital, 61250 Trabzon, Türkiye
- 45 Division of Endocrinology and Metabolism, Department of Internal Medicine, Faculty of Medicine, Akdeniz University, 07070 Antalya, Türkiye
- 46 Department of Internal Medicine, Faculty of Medicine, Akdeniz University, 07070 Antalya, Türkiye
- 47 Adana Dr Turgut Noyan Teaching and Research Center, Department of Nephrology, Faculty of Medicine, Baskent University, 06790 Adana, Türkiye
- 48 Nephrology Clinic, Bursa Yüksek İhtisas Training and Research Hospital, Health Sciences University, 16310 Bursa, Türkiye
- 49 Nephrology Clinic, Bursa Yüksek İhtisas Training and Research Hospital, 16310 Bursa, Türkiye
- 50 Nephrology Clinic, Faculty of Medicine, Giresun University, 28200 Giresun, Türkiye
- 51 Department of Nephrology, Bursa Acıbadem Hospital, 16210 Bursa, Türkiye
- 52 Division of Nephrology, Department of Internal Medicine, Afyonkarahisar Health Sciences University, 03030 Afyonkarahisar, Türkiye
- 53 Department of Nephrology, Kahramanmaraş Necip Fazıl City Hospital, 46050 Kahramanmaraş, Türkiye
- 54 Karabük Training and Research Hospital, 78200 Karabük, Türkiye
- 55 Department of Nephrology, Balıkesir Atatürk City Hospital, 10100 Balıkesir, Türkiye
- 56 Department of Nephrology, Faculty of Medicine, Gazi University, 06560 Ankara, Türkiye
- 57 Department of Nephrology, Kocaeli City Hospital, 41060 Kocaeli, Türkiye
- 58 Division of Nephrology, Department of Internal Medicine, School of Medicine, Çanakkale Onsekiz Mart University, 17100 Çanakkale, Türkiye
- 59 Division of Nephrology, Department of Internal Medicine, Faculty of Medicine, Recep Tayyip Erdoğan University, 53100 Rize, Türkiye
- 60 Burdur State Hospital, 15100 Burdur, Türkiye
- 61 Department of Nephrology, Şişli Hamidiye Etfal Training and Research Hospital, 34371 İstanbul, Türkiye
- 62 Nephrology Clinic, Kütahya Evliya Çelebi Education and Research Hospital, 43040 Kütahya, Türkiye
- 63 Department of Cardiology, Faculty of Medicine, Memorial Göztepe Hospital, Bahçeşehir University, 34349 İstanbul, Türkiye
- 64 Department of Nephrology, Sultan Abdülhamid Han Training and Research Hospital, Health Sciences University, 34668 İstanbul, Türkiye
- 65 Department of Nephrology, Health Sciences University Kocaeli City Hospital, 41060 Kocaeli, Türkiye; dr.erkansengul@hotmail.com
- 66 Department of Nephrology, Health Sciences University Kartal Dr Lütfi Kırdar City Hospital, 34865 İstanbul, Türkiye; elifaribakir@gmail.com

* Correspondence: alper.tuna.guven@gmail.com

Abstract

Background/Objectives: Finerenone improves cardiovascular and renal outcomes in diabetic kidney disease (DKD), but hyperkalemia remains a key safety concern. Patients with elevated baseline potassium levels (≥ 4.9 mEq/L) are largely excluded from clinical trials, and real-world data in this population are scarce. **Methods:** In this retrospective multicenter cohort study derived from the FINE-TURK cohort, adults with DKD who initiated finerenone with baseline potassium ≥ 4.9 mEq/L were included. The primary outcome was clinically significant hyperkalemia ($K \geq 5.5$ mEq/L) within three months. Multivariable logistic regression analyses were used to identify associated factors, with multiple sensitivity analyses performed. **Results:** A total of 166 patients were included, of whom 47 (28.3%) had baseline potassium levels between 5.1 and 5.5 mEq/L. Of the 166 patients, 35 (21.1%) reached the primary outcome, and 10 (6%) patients had follow-up potassium ≥ 6.0 mEq/L. 126 (76.8%) patients required no intervention, 24 (14.6%) were initiated on potassium binders, and finerenone was discontinued in only 12 (7.3%) patients. Lower baseline estimated glomerular filtration rate, baseline urinary albumin, loop diuretic use and 20 mg finerenone dose were associated with the primary outcome. In contrast, baseline potassium was not associated with the primary outcome. **Conclusions:** In patients with DKD and elevated baseline potassium levels, finerenone initiation was associated with manageable rates of hyperkalemia. Our findings support the cautious use of finerenone in selected patients under close monitoring, as well as highlight the need for a multidimensional approach to hyperkalemia risk assessment.

Keywords: diabetes complications; diabetic nephropathies; hyperkalemia; mineralocorticoid receptor antagonists; retrospective study

1. Introduction

Type 2 diabetes (T2D) and diabetic kidney disease (DKD) represent a major and growing global health burden, contributing substantially to cardiovascular and renal morbidity and mortality, collectively known as cardio-renal-metabolic (CRM) disease. Globally, approximately 40% of individuals with type 2 diabetes develop diabetic kidney disease, making diabetes the leading cause of chronic kidney disease worldwide [1–4]. Over the past decades, significant therapeutic advances—particularly with renin-angiotensin-aldosterone system (RAAS) inhibitors, including angiotensin-converting enzyme inhibitors (ACEi) and angiotensin receptor blockers (ARBs), as well as sodium-glucose cotransporter-2 (SGLT2) inhibitors—have markedly improved cardiovascular and renal outcomes in this population [5–9]. Despite these therapeutic advances, a considerable residual risk of kidney disease progression and cardiovascular events persists, underscoring the importance of early identification, comprehensive risk assessment, and the development of additional therapies targeting complementary pathophysiological pathways [10].

Due to increased aldosterone activity in CRM diseases, steroidal mineralocorticoid receptor antagonists (MRAs) such as spironolactone and eplerenone play a significant role in the management of heart failure; however, their use has been largely limited by the risk of hyperkalemia in chronic kidney disease (CKD) [11]. Finerenone, a novel nonsteroidal MRA, has demonstrated significant renal and cardiovascular benefits in patients with DKD in large randomized controlled trials [12,13]. Importantly, compared with steroidal MRAs, finerenone has been associated with a more favorable safety profile with respect

to hyperkalemia [14,15]. Nevertheless, hyperkalemia remains one of the most clinically relevant adverse effects and continues to influence prescribing decisions, especially in patients with impaired kidney function or elevated baseline potassium levels. The pivotal trials of finerenone, including FIDELIO-DKD and FIGARO-DKD [12,13], largely excluded patients with higher baseline potassium levels (i.e., potassium ≥ 4.9 mEq/L), and current prescribing recommendations on the manufacturer's label, which are derived from the aforementioned trials, reflect similar criteria [16]. As a result, only selected patients with borderline hyperkalemia (i.e., potassium ≥ 4.9 mEq/L) are initiated on finerenone, and patients with mild hyperkalemia (i.e., potassium ≥ 5.1 mEq/L) are not initiated on finerenone at all. These scenarios are frequently encountered in routine clinical practice, creating a gap between trial-based recommendations and real-world decision-making. Consequently, clinicians frequently face uncertainty when balancing the potential cardiorenal benefits of finerenone against concerns regarding hyperkalemia in patients who would have been excluded from pivotal clinical trials. Meanwhile, prior analyses [14], including our earlier work from the FINE-TURK cohort [17], have identified baseline potassium and estimated glomerular filtration rate (eGFR) as key determinants of hyperkalemia risk in a general DKD population. Whether these associations remain applicable in patients with elevated baseline potassium levels remains uncertain. Therefore, the primary objective of the present study was to evaluate the incidence of clinically significant hyperkalemia following finerenone initiation in patients with DKD and elevated baseline potassium levels. The secondary objectives were to characterize potassium management strategies during follow-up and to identify baseline factors independently associated with clinically significant hyperkalemia.

2. Materials and Methods

2.1. Study Design and Population

This study was designed as a retrospective cohort analysis derived from the FINE-TURK cohort, a national, multicenter cohort evaluating the real-world use of finerenone in patients with DKD who receive contemporary CRM treatments. The design and overall characteristics of the FINE-TURK cohort have been described previously [18]. For the present analysis, a subgroup of patients from the FINE-TURK cohort was evaluated. Adult patients (≥ 18 years) with T2D and DKD, with baseline potassium ≥ 4.9 mEq/L, who initiated finerenone, were eligible. Patients were eligible if baseline potassium, baseline estimated glomerular filtration rate (eGFR, calculated using the CKD-EPI equation), and at least one follow-up potassium measurement within three months of finerenone initiation were available. If more than one potassium measurement was available, the higher potassium value was chosen as the follow-up potassium value to implement a conservative, worst-case approach to hyperkalemia ascertainment.

The present study represents a distinct prespecified subgroup analysis of the FINE-TURK cohort, specifically focusing on patients with elevated baseline potassium levels (≥ 4.9 mEq/L). This population was not included in our previous FINE-TURK analysis [17], which evaluated finerenone-associated hyperkalemia in patients with baseline potassium ≤ 4.8 mEq/L and more closely reflected the eligibility criteria of pivotal finerenone trials.

2.2. Variables of Interest

The following variables were extracted from electronic medical records: age, sex, systolic blood pressure (BP), diastolic BP, body mass index (BMI), clinician-diagnosed or patient-reported comorbidities of hypertension, coronary artery disease (CAD, defined as history of myocardial infarction or revascularization), stroke, and diabetic retinopathy (DRP); finerenone dose initiated (20 mg or 10 mg); current use of any SGLT2 inhibitor, use

of any ACE inhibitor or ARB, presence of maximal RAAS inhibition (according to manufacturers' labels), use of any glucagon-like peptide-1 (GLP-1) receptor agonist, dipeptidyl peptidase-4 (DPP-4) inhibitors, current use of any insulin, metformin, sulfonylurea, calcium channel blocker, beta blocker, alpha blocker, thiazide (or thiazide-like) diuretic, loop diuretic, any antihypertensive, and statin. Regarding laboratory tests, baseline eGFR, baseline serum potassium, baseline urinary albumin (mg/g creatinine), baseline urinary protein (mg/g creatinine), baseline serum sodium, baseline serum albumin, baseline serum uric acid, baseline hemoglobin, and baseline hemoglobin A1c (HbA1c) values were acquired. Baseline potassium levels were dichotomized into 4.9–5.0 mEq/L and 5.1–5.5 mEq/L for further analysis. The former represents the group for borderline hyperkalemia, for whom the manufacturer's label states finerenone initiation may be considered according to patient characteristics with close potassium follow-up. The latter represents patients with mild hyperkalemia, for whom finerenone is not recommended according to the manufacturer's prescribing information.

2.3. Outcome Definition

The primary outcome was clinically significant hyperkalemia, defined as a follow-up potassium level of ≥ 5.5 mEq/L, within three months of finerenone initiation. Secondary outcomes included potassium-lowering interventions, bicarbonate therapy, finerenone discontinuation, and the distribution of follow-up potassium categories. The potassium threshold was selected based on the manufacturer's label and contemporary clinical guidelines, which recommend treatment cessation at potassium levels ≥ 5.5 mEq/L. In addition, follow-up potassium levels were also analyzed as an ordinal variable, categorized as <5.0 , 5.0 – 5.4 , 5.5 – 5.9 , and ≥ 6.0 mEq/L. This approach was used to better characterize the distribution and severity of hyperkalemia in the cohort and to capture clinically relevant gradients of risk beyond a single threshold. Furthermore, hyperkalemia management strategies, including no intervention, initiation of potassium binders, finerenone discontinuation, and initiation of bicarbonate therapy, were evaluated and grouped according to follow-up potassium levels.

2.4. Statistical Analysis

Continuous variables were assessed for normality using the Shapiro–Wilk test. No variables were distributed normally, and non-normally distributed variables were presented as medians with interquartile ranges. Between-group comparisons of continuous variables were performed using the Mann–Whitney U test. Categorical variables were shown as counts and percentages, and between-group comparisons were performed using the chi-square test. To evaluate factors associated with clinically significant hyperkalemia, logistic regression (LR) analyses were performed. Univariate LR analyses were initially conducted to assess crude associations between candidate variables and clinically significant hyperkalemia. Covariates included in the multivariable model were selected a priori based on biological plausibility, existing literature, and findings from previous analyses of the FINE-TURK cohort rather than solely on univariate statistical significance. The final model included baseline potassium, baseline eGFR, log-transformed baseline urinary albumin, finerenone dose, and loop diuretic use. Given the limited number of outcome events, the number of covariates included in each multivariable model was restricted to minimize overfitting, in accordance with events-per-variable principles. Baseline potassium was modeled as a continuous variable and scaled per 0.1 mEq/L increase to facilitate clinical interpretation of effect estimates. Baseline urinary albumin and protein were logarithmically transformed because of their right-skewed distributions. Finerenone dose and loop diuretic use were analyzed as binary variables. Results are presented as odds ratios (ORs) with

corresponding 95% confidence intervals (CIs). Model calibration was evaluated using the Hosmer–Lemeshow goodness-of-fit test, and model discrimination was assessed by calculating the area under the receiver operating characteristic curve. To evaluate the robustness of the findings, prespecified sensitivity analyses were performed using alternative model specifications, including substitution of baseline urinary albumin with baseline urinary protein, replacement of loop diuretic use with diabetic retinopathy status, replacement of loop diuretic use with thiazide diuretic use, and removing loop diuretics from the model. Observations with missing values for variables included in a given analysis were excluded from that specific analysis (complete-case analysis). A two-sided p value < 0.05 was considered statistically significant. All statistical analyses were performed using IBM SPSS Statistics, version 25 (IBM Corp., Armonk, NY, USA).

3. Results

3.1. Study Population and Baseline Characteristics

A total of 166 patients with DKD and baseline potassium ≥ 4.9 mEq/L were included. The median age was 61.5 (54–70) years, and 51.2% were female. The median baseline potassium level was 5.0 (4.9–5.1) mEq/L. When stratified by baseline potassium categories, patients with mild hyperkalemia had higher BMI (30.9 vs. 28.4, $p = 0.008$) and lower diastolic BP (76 vs. 80, $p = 0.023$) compared to borderline hyperkalemic patients. They also exhibited significantly higher levels of baseline urinary albumin (1900 vs. 949, $p = 0.018$) and baseline urinary protein (2269 vs. 1423, $p = 0.044$). Initiation of finerenone at 20 mg was also more frequent in patients with baseline mild hyperkalemia (12.8% vs. 2.5%, $p = 0.009$), although the absolute number of patients receiving 20 mg was small (6 vs. 3). When patients were stratified according to follow-up potassium levels, clinically significant hyperkalemia occurred in 35 patients (21.1%). Patients who developed clinically significant hyperkalemia had lower baseline eGFR (39 vs. 47, $p = 0.011$) and higher levels of baseline urinary albumin (3096 vs. 903, $p < 0.001$) and baseline urinary protein levels (4260 vs. 1419, $p = 0.001$). DRP was more frequent (66.7% vs. 45.8%, $p = 0.041$), and loop diuretic use was more common in patients who developed clinically significant hyperkalemia (31.4% vs. 12.6%, $p = 0.008$). Table 1 summarizes the baseline characteristics according to baseline potassium categories and follow-up hyperkalemia status in detail.

3.2. Potassium Trajectory and Distribution

The median follow-up potassium level was 5.1 (4.9–5.4) mEq/L. Patients with baseline mild hyperkalemia had higher follow-up potassium values compared to borderline hyperkalemic patients (5.2 vs. 5.0 mEq/L, $p = 0.003$). However, the magnitude of potassium change did not differ significantly between baseline potassium groups (0.1 vs. 0.1, $p = 0.162$) (Table 2). When categorized ordinally, 46 (27.7%) patients had follow-up potassium levels < 5.0 mEq/L, 85 (51.2%) had levels of 5.0–5.4 mEq/L, 25 (15.1%) had levels of 5.5–5.9 mEq/L, and 10 (6.0%) had levels ≥ 6.0 mEq/L. Patients with baseline mild hyperkalemia levels approached statistical significance with a shift toward higher follow-up potassium categories ($p = 0.052$). Table 2 summarizes the distribution of follow-up potassium levels according to baseline potassium categories in detail.

Table 1. Baseline patient characteristics according to baseline potassium categories and follow-up hyperkalemia status.

	Total (N = 166)	Baseline Potassium			Follow-Up Potassium		
		K = 4.9–5.0 (N = 119)	K = 5.1–5.5 (N = 47)	<i>p</i> *	K < 5.5 (N = 131)	K ≥ 5.5 (N = 35)	<i>p</i> *
Demographics and Physical Examination							
Age	61.5 (54–70)	61 (54–70)	62 (54–69)	0.87	62 (54–69)	59 (54–71)	0.804
Sex							
Female	85 (51.2%)	58 (48.7%)	27 (57.4%)	0.312	66 (50.4%)	19 (54.3%)	0.681
Male	81 (48.8%)	61 (51.3%)	20 (42.6%)		65 (49.6%)	16 (45.7%)	
BMI	29.1 (26.3–33.0)	28.4 (25.7–32.7)	30.9 (28–33.3)	0.008	29.0 (25.8–33)	29.4 (26.9–33.1)	0.664
Systolic BP	130 (125–144)	130 (127–140)	132 (123–149)	0.786	130 (125–140)	140 (130–154)	0.096
Diastolic BP	80 (72–88)	80 (75–90)	76 (70–80)	0.023	80 (70–88)	80 (73–89)	0.575
Comorbidities							
Hypertension	155 (93.4%)	111 (93.3%)	44 (93.6%)	0.937	120 (91.6%)	35 (100%)	0.076
CAD	61 (37.2%)	45 (38.5%)	16 (34%)	0.597	50 (38.8%)	11 (31.4%)	0.426
Stroke	19 (11.7%)	14 (12.1%)	5 (10.6%)	0.797	15 (11.6%)	4 (11.8%)	0.982
DRP	75 (50%)	52 (48.1%)	23 (54.8%)	0.467	55 (45.8%)	20 (66.7%)	0.041
RAS Inhibitors							
ACE inhibitor	65 (39.4%)	46 (38.7%)	19 (41.3%)	0.755	51 (39.2%)	14 (40%)	0.934
ARB	80 (48.5%)	56 (47.1%)	24 (52.2%)	0.556	64 (49.2%)	16 (45.7%)	0.712
Maximal RAAS blockade	105 (67.3%)	78 (69%)	27 (62.8%)	0.458	82 (66.7%)	23 (69.7%)	0.742
SGLT-2 Inhibitors and GLP-1 Receptor Agonists							
SGLT-2 inhibitor	142 (85.5%)	100 (84%)	42 (89.4%)	0.379	114 (87%)	28 (80%)	0.294
GLP-1 receptor agonist	1 (0.6%)	0	1 (2.1%)	0.283	1 (0.8%)	0	1

Table 1. Cont.

	Total	Baseline Potassium			Follow-Up Potassium		
	(N = 166)	K = 4.9–5.0 (N = 119)	K = 5.1–5.5 (N = 47)	<i>p</i> *	K < 5.5 (N = 131)	K ≥ 5.5 (N = 35)	<i>p</i> *
Finerenone							
Finerenone dose							
10 mg	157 (94.6%)	116 (97.5%)	41(87.2%)	0.009	126 (96.2%)	31 (88.6%)	0.095
20 mg	9 (5.4%)	3 (2.5%)	6 (12.8%)		5 (3.8%)	4 (11.4%)	
Other Glucose-Lowering Medications							
DPP-4 inhibitor	99 (59.6%)	70 (58.8%)	29 (61.7%)	0.733	79 (60.3%)	20 (57.1%)	0.735
Insulin	90 (56.3%)	61 (53%)	29 (64.4%)	0.191	70 (56%)	20 (57.1%)	0.904
Metformin	70 (42.2%)	51 (42.9%)	19 (40.4%)	0.775	57 (43.5%)	13 (37.1%)	0.498
Sulfonylurea	8 (4.8%)	5 (4.2%)	3 (6.4%)	0.554	5 (3.8%)	3 (8.6%)	0.367
Anti-Hypertensive Medications							
CCB	84 (50.9%)	59 (49.6%)	25 (54.3%)	0.583	61 (46.9%)	23 (65.7%)	0.048
Beta-blocker	75 (45.5%)	48 (40.3%)	27 (58.7%)	0.034	58 (44.6%)	17 (48.6%)	0.677
Alpha-blocker	20 (12.1%)	13 (10.9%)	7 (15.2%)	0.449	14 (10.8%)	6 (17.1%)	0.305
Thiazide	64 (38.8%)	41 (34.5%)	23 (50%)	0.066	52 (40%)	12 (34.3%)	0.538
Loop diuretics	27 (16.7%)	17 (14.3%)	10 (23.3%)	0.176	16 (12.6%)	11 (31.4%)	0.008
Any anti-hypertensive	160 (96.4%)	114 (95.8%)	46 (97.9%)	0.519	125 (95.4%)	35 (100%)	0.197
Lipid-Lowering Medications							
Statin	100 (60.6%)	70 (59.3%)	30 (63.8%)	0.593	80 (61.1%)	20 (58.8%)	0.811

Table 1. Cont.

	Total	Baseline Potassium			Follow-Up Potassium		
	(N = 166)	K = 4.9–5.0 (N = 119)	K = 5.1–5.5 (N = 47)	<i>p</i> *	K < 5.5 (N = 131)	K ≥ 5.5 (N = 35)	<i>p</i> *
	Laboratory						
Baseline potassium (mEq/L)	5.0 (4.9–5.1)	4.9 (4.9–5.0)	5.2 (5.1–5.3)	<0.001	4.9 (4.9–5.1)	5.0 (5.0–5.1)	0.007
Baseline eGFR (mL/min/1.73m ²)	44 (34–57)	45 (36–58)	41 (32–55)	0.128	47 (36–60)	39 (32–46)	0.011
Baseline urinary albumin (mg/g creatinine)	1392 (373–2901)	949 (247–2370)	1900 (805–4349)	0.018	903 (258–2105)	3096 (1527–4808)	<0.001
Baseline urinary protein (mg/g creatinine)	1950 (732–4194)	1423 (610–3400)	2269 (1192–5779)	0.044	1419 (660–3142)	4260 (1220–6717)	0.001
Baseline serum sodium (mEq/L)	139 (137–141)	139 (138–141)	139 (137–141)	0.947	139 (138–141)	138 (137–142)	0.833
Baseline serum albumin (g/dL)	4.1 (3.9–4.3)	4.1 (3.9–4.3)	4.1 (3.8–4.5)	0.619	4.1 (3.9–4.3)	4.0 (3.5–4.3)	0.356
Baseline serum uric acid (mg/dL)	6.4 (5.5–7.5)	6.5 (5.6–7.5)	6.4 (5.2–7.4)	0.564	6.4 (5.3–7.4)	6.7 (5.6–7.6)	0.430
Baseline HbA1c (%)	7.6 (6.7–8.4)	7.4 (6.6–8.4)	7.9 (7–8.5)	0.138	7.6 (6.7–8.4)	7.4 (6.6–8.4)	0.776

ACE: Angiotensin-converting enzyme, ARB: Angiotensin receptor blocker, BMI: Body mass index, BP: Blood pressure, CAD: Coronary artery disease, CCB: Calcium channel blocker, DPP-4: Dipeptidyl peptidase-4, DRP: Diabetic retinopathy, eGFR: Estimated glomerular filtration rate, GLP-1: Glucagon-like peptide-1, HbA1c: Glycated hemoglobin, K: Potassium, RAAS: Renin–angiotensin–aldosterone system, SGLT-2: Sodium-glucose transporter-2. * *p* values with statistical significance are shown in bold.

Table 2. Distribution of follow-up potassium levels according to baseline potassium categories.

	Total	Baseline Potassium		<i>p</i> *
	(N = 166)	K = 4.9–5.0 (N = 119)	K = 5.1–5.5 (N = 47)	
Follow-up potassium (mEq/L)	5.1 (4.9–5.4)	5 (4.9–5.3)	5.2 (5.1–5.5)	0.003
Potassium change	0.1 (0–0.4)	0.1 (0–0.4)	0.1 (–0.1–0.2)	0.162
Follow-up potassium (Ordinal)				
<5.0 (mEq/L)	46 (27.7%)	40 (33.6%)	6 (12.8%)	0.052
5.0–5.4 (mEq/L)	85 (51.2%)	58 (48.7%)	28 (59.6%)	
5.5–5.9 (mEq/L)	25 (15.1%)	15 (12.6%)	9 (19.1%)	
≥6.0 (mEq/L)	10 (6%)	6 (5%)	4 (8.5%)	

K: Potassium. * *p* values with statistical significance are shown in bold.

3.3. Hyperkalemia Management

Data on hyperkalemia management were missing for 2 patients; therefore, hyperkalemia management analysis was conducted on 164 patients. Overall, no intervention was required in 76.8% of patients. Follow-up potassium levels were associated with different intervention strategies ($p < 0.001$). Among patients with follow-up potassium levels of 5.5–5.9 mEq/L, potassium binders were initiated in 65.2%, and finerenone was discontinued only in 13% of patients. However, in patients with follow-up potassium levels ≥ 6.0 mEq/L, finerenone was discontinued in all cases. Bicarbonate therapy was infrequently used and limited to two patients with moderate hyperkalemia. Table 3 summarizes the management strategies and treatment modifications following hyperkalemia in detail.

Table 3. Management strategies and treatment modifications following hyperkalemia.

Management for Follow-Up Potassium Levels	Total	Follow-Up Potassium			
	(N = 164 *)	<5.0 (mEq/L) (N = 46)	5.0–5.4 (mEq/L) (N = 86)	5.5–5.9 (mEq/L) (N = 23)	≥6.0 (mEq/L) (N = 9)
No intervention	126 (76.8%)	46 (100%)	77 (89.5%)	3 (13%)	0
Potassium binder initiation	24 (14.6%)	0	9 (10.5%)	15 (65.2%)	0
Finerenone cessation	12 (7.3%)	0	0	3 (13%)	9 (100%)
Bicarbonate initiation	2 (1.2%)	0	0	2 (8.7%)	0

* 2 patients' data on hyperkalemia management were missing.

3.4. Factors Associated with Clinically Significant Hyperkalemia

In univariate LR analysis (Figure 1), baseline potassium, baseline eGFR, DRP, baseline urinary albumin (log-transformed) and protein, and loop diuretic use were associated with clinically significant hyperkalemia. Thiazide use and finerenone dose were not associated with clinically significant hyperkalemia in univariate logistic regression analysis. In multivariable logistic regression analysis (Figure 2), baseline potassium was not independently associated with clinically significant hyperkalemia (OR 1.026, 95% CI 0.737–1.429, $p = 0.879$). Conversely, lower baseline eGFR (OR 0.966, 95% CI 0.934–0.998, $p = 0.040$), higher baseline urinary albumin (log-transformed; OR 2.837, 95% CI 1.199–6.716, $p = 0.018$), loop diuretic use (OR 3.118, 95% CI 1.005–9.678, $p = 0.049$), and initiation with a 20 mg finerenone dose (OR 16.354, 95% CI 2.245–119.115, $p = 0.006$) were independently associated with clinically significant hyperkalemia. The model demonstrated moderate explanatory performance (Nagelkerke $R^2 = 0.274$), acceptable goodness-of-fit according to the Hosmer–Lemeshow test ($\chi^2 = 11.985$, $df = 8$, $p = 0.152$) and acceptable discrimination, with an area under the receiver operating characteristic curve of 0.790 (95% CI, 0.686–0.894; $p < 0.001$). Table 4

demonstrates the factors associated with hyperkalemia in univariate and multivariable LR analyses in detail.

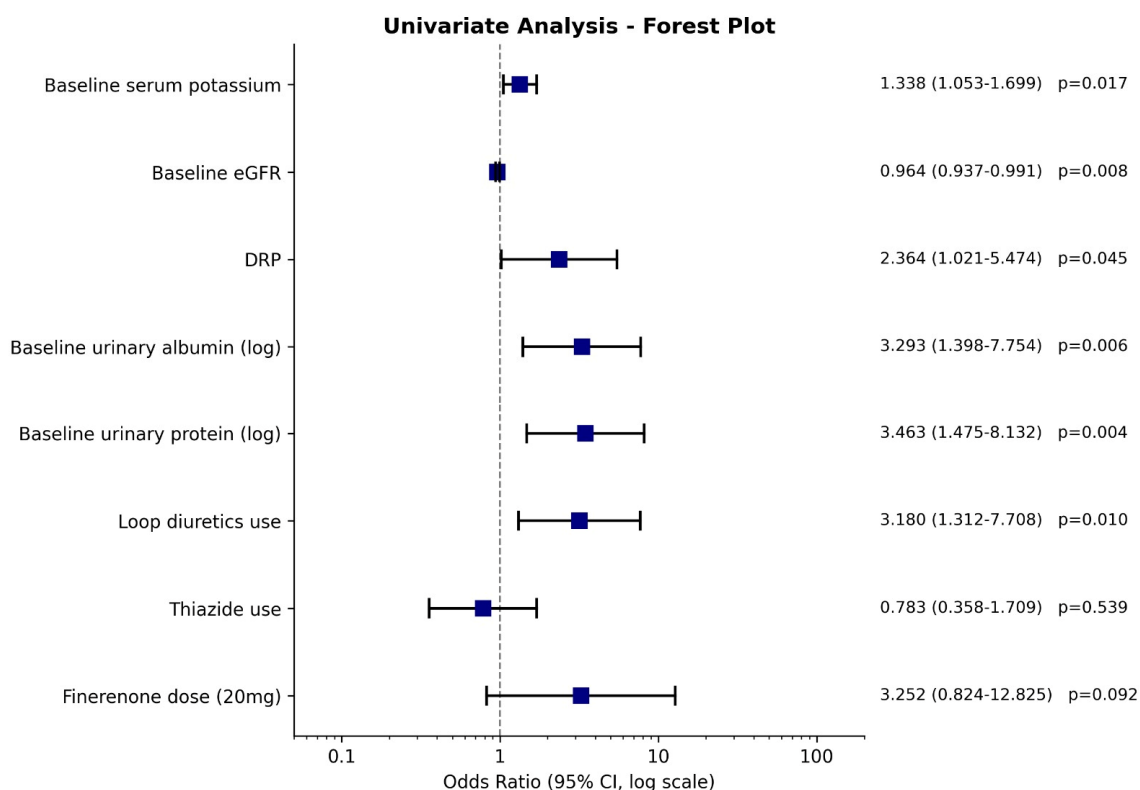


Figure 1. Forest plot of factors associated with clinically significant hyperkalemia in univariate logistic regression analyses. CI: Confidence interval, DRP: Diabetic retinopathy, eGFR: Estimated glomerular filtration rate.

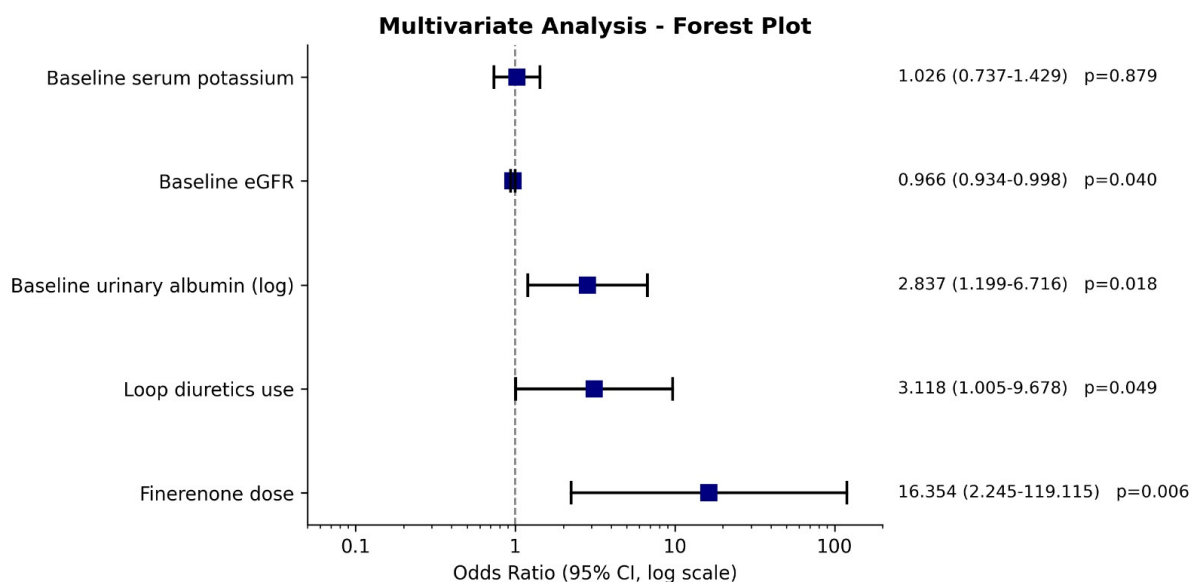


Figure 2. Forest plot of factors associated with clinically significant hyperkalemia in multivariable logistic regression analyses. CI: Confidence interval, eGFR: Estimated glomerular filtration rate.

Table 4. Factors associated with hyperkalemia: Univariate and multivariable logistic regression analyses.

Univariate Analysis		
	OR (95%CI)	<i>p</i> *
Baseline potassium	1.338 (1.053–1.699)	0.017
Baseline eGFR	0.964 (0.937–0.991)	0.008
DRP	2.364 (1.021–5.474)	0.045
Baseline urinary albumin (log-transformed)	3.293 (1.398–7.754)	0.006
Baseline urinary protein (log-transformed)	3.463 (1.475–8.132)	0.004
Loop diuretics use	3.180 (1.312–7.708)	0.010
Thiazide use	0.783 (0.358–1.709)	0.539
Finerenone dose (20 mg)	3.252 (0.824–12.825)	0.092
Multivariate Analysis		
	OR (95%CI)	<i>p</i> *
Baseline potassium	1.026 (0.737–1.429)	0.879
Baseline eGFR	0.966 (0.934–0.998)	0.040
Baseline urinary albumin (log-transformed)	2.837 (1.199–6.716)	0.018
Loop diuretics use	3.118 (1.005–9.678)	0.049
Finerenone dose	16.354 (2.245–119.115)	0.006
Nagelkerke $R^2 = 0.274$, Hosmer–Lemeshow goodness-of-fit: $\chi^2 = 11.985$, $df = 8$, $p = 0.152$. AUC = 0.790 (95% CI, 0.686–0.894).		

AUC: Area under the receiver operating characteristic curve; CI: Confidence interval; DRP: Diabetic retinopathy; eGFR: Estimated glomerular filtration rate; OR: Odds ratio. * *p* values with statistical significance are shown in bold.

3.5. Sensitivity Analyses

Sensitivity analyses using alternative multivariable model specifications demonstrated overall robustness of the findings (Table 5). Replacement of baseline urinary albumin with baseline urinary protein yielded comparable results, with lower eGFR, higher baseline urinary protein, and 20 mg finerenone dose remaining independently associated with clinically significant hyperkalemia, whereas baseline potassium and loop diuretic use were not associated. Similarly, replacing loop diuretic use with diabetic retinopathy and thiazide diuretic use did not materially alter the results, with baseline urinary albumin and 20 mg finerenone dose remaining significant factors, while baseline potassium, diabetic retinopathy and thiazide diuretic use were not associated with hyperkalemia. In an additional model excluding loop diuretic use, lower baseline eGFR, higher baseline urinary albumin excretion, and 20 mg finerenone dose remained independently associated with clinically significant hyperkalemia. Across all sensitivity analyses, baseline potassium consistently lacked an independent association with clinically significant hyperkalemia, whereas the association between 20 mg finerenone dose and hyperkalemia remained robust.

Table 5. Sensitivity analyses of multivariable models for factors associated with hyperkalemia.

Model 1	OR (95%CI)	<i>p</i> *
Baseline potassium	1.064 (0.795–1.425)	0.677
Baseline eGFR	0.960 (0.931–0.990)	0.010
Baseline urinary protein (log-transformed)	3.474 (1.339–9.014)	0.010
Loop diuretics use	1.712 (0.614–4.770)	0.304
Finerenone dose	17.773 (2.358–133.964)	0.005
Nagelkerke $R^2 = 0.248$		
Model 2	OR (95%CI)	<i>p</i> *
Baseline potassium	1.049 (0.754–1.459)	0.779
Baseline eGFR	0.974 (0.943–1.006)	0.114
Baseline urinary albumin (log-transformed)	3.252 (1.202–8.797)	0.020
DRP	1.414 (0.487–4.102)	0.524
Finerenone dose	15.630 (1.157–211.206)	0.038
Nagelkerke $R^2 = 0.183$		
Model 3	OR (95%CI)	<i>p</i> *
Baseline potassium	1.066 (0.774–1.468)	0.695
Baseline eGFR	0.961 (0.930–0.992)	0.015
Baseline urinary albumin (log-transformed)	3.302 (1.353–8.058)	0.009
Finerenone dose	15.437 (2.116–112.630)	0.007
Nagelkerke $R^2 = 0.240$		
Model 4	OR (95%CI)	<i>p</i> *
Baseline potassium	1.086 (0.784–1.503)	0.619
Baseline eGFR	0.960 (0.930–0.992)	0.013
Baseline urinary albumin (log-transformed)	3.322 (1.355–8.142)	0.009
Thiazide diuretics use	0.692 (0.254–1.885)	0.471
Finerenone dose	14.103 (1.910–104.159)	0.009
Nagelkerke $R^2 = 0.246$		

CI: Confidence interval; DRP: Diabetic retinopathy; eGFR: Estimated glomerular filtration rate; OR: Odds ratio.
 * *p* values with statistical significance are shown in bold.

4. Discussion

In this multicenter retrospective cohort analysis derived from the FINE-TURK cohort, we evaluated potassium dynamics, management strategies, and factors associated with clinically significant hyperkalemia in patients with DKD who were initiated on finerenone despite borderline or mild hyperkalemia. This represents a clinically relevant yet significantly understudied population that is largely, if not totally, excluded from randomized trials [12,13,19]. Clinically significant hyperkalemia occurred in approximately one-fifth of patients; however, most cases were mild and manageable, and the majority of patients did not require treatment cessation. Importantly, in contrast to patients with baseline potassium levels ≤ 4.8 mEq/L [14,17], baseline potassium was not independently associated with clinically significant hyperkalemia, whereas baseline urinary albumin demonstrated a more consistent association. These apparently differing observations should not be interpreted as contradictory findings but rather as complementary evidence derived from distinct clinical populations. While our previous FINE-TURK analysis [17] evaluated patients with

baseline potassium levels within the conventional finerenone initiation range, the present study specifically focused on patients with elevated baseline potassium levels who were largely excluded from randomized clinical trials. Therefore, the determinants of finerenone-associated hyperkalemia may differ between these two clinically distinct scenarios. To the best of our knowledge, this is the first real-world study specifically evaluating finerenone-associated hyperkalemia in patients with elevated baseline potassium levels—a population largely excluded from clinical trials.

The percentages of patients experiencing potassium levels > 5.5 mEq/L and >6.0 mEq/L were 21.4% and 4.5%, respectively, in the FIDELIO-DKD trial and 13.5% and 2.3%, respectively, in the FIGARO-DKD trial [12–14]. However, observational FINE-REAL study and a recent cohort study using the FOUNTAIN platform demonstrated that potassium levels > 5.5 mEq/L were observed in only 8% and 1.2% of the patients, respectively [20,21]. These rates are similar to our group's recent study [17], in which similar eligibility criteria to landmark trials were used, which demonstrated that potassium levels ≥ 5.5 mEq/L were observed only in 7.3% of the patients. Our current study demonstrated that potassium levels > 5.5 mEq/L and >6.0 mEq/L were almost similar to findings from the FIDELIO-DKD trial [13], indicating a risk profile comparable to that observed in clinical trials. The observed difference in hyperkalemia between clinical trials and observational studies may be explained by exceedingly low SGLT2 inhibitor utilization in landmark trials (4.4% and 8.5% in the FIDELIO-DKD and the FIGARO-DKD, respectively, vs. 38.0% in the FOUNTAIN platform study and 89% in our previous study) and a higher rate of the 10 mg finerenone dose in cohort studies compared to 20 mg dose (85% in both the FOUNTAIN platform study and the FINE-REAL study and 83% in our previous study).

Analyzing the factors associated with clinically significant hyperkalemia yielded several unexpected findings that contrasted with published literature data. Our previous study [17] had demonstrated that baseline potassium, baseline eGFR and finerenone dose were the most prominent factors associated with hyperkalemia, followed by thiazide diuretic use. Similarly, post hoc safety analysis of the FIDELIO-DKD trial, and the FOUNTAIN platform study indicated that baseline potassium, baseline eGFR, diuretic use, SGLT2 inhibitor use, and baseline urinary albumin were associated with hyperkalemia [14,20]. However, baseline potassium and thiazide diuretics were not associated with clinically significant hyperkalemia in the current study, and loop diuretics use was associated with clinically significant hyperkalemia. There may be several explanations for these findings. Firstly, approximately three-quarters of the patients in our study had baseline potassium levels of either 4.9 mEq/L or 5 mEq/L. The limited variability in potassium concentrations may have reduced its discriminatory ability as an independent variable. Therefore, the absence of an independent association between baseline potassium and clinically significant hyperkalemia should be interpreted cautiously and it should not be interpreted as indicating that baseline potassium lacks prognostic value in broader DKD populations. Secondly, association of loop diuretics and clinically significant hyperkalemia may reflect confounding by indication, as loop diuretics are more frequently prescribed in patients with advanced CKD, volume overload, or concomitant heart failure [22]. Therefore, loop diuretic use may act as a surrogate marker of disease severity rather than an independent causal factor, since biological causality would be expected in the reverse direction, namely, association with lower odds of hyperkalemia. Taken together, these findings suggest that the determinants of hyperkalemia are context-dependent and may not be generalizable for each baseline potassium and CKD severity level. This pattern mirrors the contemporary classification of CKD, which integrates both eGFR and albuminuria rather than relying on either parameter alone [22]. Similarly, our findings suggest that finerenone-

associated hyperkalemia risk is not driven by a single parameter but rather emerges from a multidimensional interplay between various markers.

From a clinical perspective, our findings provide reassurance regarding the safety profile of finerenone in patients with borderline or mild hyperkalemia. Although rates of drug discontinuation in our cohort were higher (7.3%) than those reported in the landmark trials of FIDELIO-DKD (2.3%) and FIGARO-DKD (1.2%), this likely reflects real-world practice patterns, including more conservative decision-making in response to rising potassium levels, as well as an already higher baseline potassium starting point. It is of particular importance to note that 13.6% of the patients in the FIDELIO-DKD trial had baseline potassium > 4.8 mEq/L, and 6.9% had baseline potassium > 5 mEq/L, similar to our study's eligibility criteria. Similarly, 4.9% of the patients in the FINE-REAL observational study had baseline potassium > 5.0 mEq/L. However, clinically significant hyperkalemia rates, factors associated with clinically significant rates, and management strategies including drug discontinuation were not reported in these specific subgroups [14,21]. Lastly, the observed incidence of clinically significant hyperkalemia should not be interpreted as trivial. Rather, these findings indicate that finerenone initiation in patients with elevated baseline potassium requires careful patient selection and structured potassium monitoring, while also demonstrating that most events can be managed without permanent treatment discontinuation.

Since our study evaluated potassium dynamics within the first three months of finerenone initiation, potassium elevations beyond this period may seem like a major limitation. The FIDELIO-DKD study demonstrated that finerenone elevated potassium levels by 0.23 mEq/L at month 4, and the levels remained largely stable thereafter [13]. The FIGARO-DKD study, which included DKD patients with lower disease severity, demonstrated that finerenone elevated potassium levels by 0.16 mEq/L at month 1, and potassium levels remained largely stable thereafter [12]. Moreover, a recent cohort study demonstrated that mean potassium increased by 0.1 mEq/L at 4 months of finerenone initiation and remained unchanged at 12 months (an increase of 0.1 mEq/L from baseline) [20]. Clinical trials, as well as the latter cohort data, provide assurance for our study with regard to its ability to capture clinically significant hyperkalemia, since potassium levels are expected to elevate within the first months of finerenone initiation and become stable thereafter.

Another clinically relevant finding of our study was the independent association between 20 mg finerenone dose and clinically significant hyperkalemia. Although the estimated effect size was accompanied by wide confidence intervals, reflecting the limited number of patients who started on 20 mg finerenone, this association remained directionally consistent across all sensitivity analyses. Therefore, while the precise magnitude of risk should be interpreted cautiously, our findings support a potential dose-dependent relationship between finerenone exposure and hyperkalemia risk. This observation is biologically plausible and consistent with the dose-dependent increases in potassium observed in our prior analyses from the FINE-TURK cohort [17].

Unlike previous studies evaluating broader diabetic kidney disease (DKD) populations, the present study specifically focused on patients with elevated baseline potassium levels, representing a clinically challenging population that has been largely excluded from the pivotal finerenone trials. Accordingly, our findings should be interpreted as complementary to, rather than contradictory to, the evidence derived from randomized clinical trials. Whereas the pivotal finerenone trials established the efficacy and safety of finerenone in carefully selected patients, our real-world analysis extends these observations to a higher-risk population commonly encountered in routine clinical practice, thereby helping to bridge the gap between trial eligibility and real-world treatment decisions. Importantly, because severe hyperkalemia may result in clinically significant electrocardiographic abnor-

malities and life-threatening arrhythmias, accurate identification of patients at increased risk remains essential [23]. Collectively, our findings suggest that elevated baseline potassium should not automatically preclude finerenone initiation. Instead, treatment decisions should be individualized by integrating kidney function, albuminuria, concomitant diuretic therapy, and availability of close potassium monitoring, rather than relying on baseline potassium concentration alone. Future prospective studies with standardized potassium monitoring protocols, longer follow-up, and larger numbers of patients receiving higher finerenone doses are warranted to validate these findings and further refine individualized risk prediction strategies.

5. Strengths and Limitations

Firstly, the retrospective observational design precludes causal inference and the findings remain susceptible to residual confounding. In addition, because finerenone initiation in patients with elevated baseline potassium was based on physician discretion rather than standardized treatment criteria, selection bias and confounding by indication cannot be excluded. Clinicians may have preferentially selected patients whom they considered less likely to develop severe hyperkalemia despite elevated baseline potassium levels; therefore, the present cohort may represent a selected subgroup rather than the broader population of patients with DKD and elevated baseline potassium encountered in routine clinical practice. Furthermore, treatment initiation, finerenone dose selection, potassium monitoring, and hyperkalemia management were not standardized across participating centers, reflecting real-world practice but introducing additional variability in patient management. Similarly, patients who underwent more frequent potassium monitoring may have had a greater likelihood of hyperkalemia detection, resulting in surveillance bias. Secondly, the sample size, particularly the number of clinically significant hyperkalemia events, was relatively limited, which may have reduced statistical power and contributed to imprecision in some estimates, as reflected by the wide confidence intervals for certain variables. Thirdly, the timing and frequency of potassium measurements were not standardized and could not be comprehensively evaluated in this retrospective study. Consequently, patients who underwent more frequent potassium monitoring may have had a greater likelihood of hyperkalemia detection, introducing surveillance bias. Furthermore, the use of the highest available potassium value during follow-up was intentionally chosen to provide a conservative estimate of clinically significant hyperkalemia and to minimize the risk of underestimating clinically relevant events. Finally, although initiation with the 20 mg dose was independently associated with clinically significant hyperkalemia, this finding should be interpreted cautiously because only a small number of patients received this dose, resulting in a wide confidence interval and limited precision of the effect estimate. Consequently, this observation should be considered hypothesis-generating rather than definitive and warrants confirmation in larger prospective cohorts.

Despite these limitations, the present study has several important strengths. To our knowledge, it is the first real-world study specifically evaluating finerenone-associated hyperkalemia in patients with elevated baseline potassium levels, a clinically challenging population which has been largely excluded from pivotal randomized trials. Furthermore, the multicenter design enhances the generalizability of the findings, while the use of predefined multivariable models and multiple sensitivity analyses supports the robustness and consistency of the observed associations.

6. Conclusions

In this multicenter real-world cohort, finerenone-associated clinically significant hyperkalemia in patients with diabetic kidney disease and elevated baseline potassium levels

occurred at rates comparable to those reported in pivotal clinical trials and was generally manageable without treatment discontinuation. Baseline potassium was not independently associated with hyperkalemia risk, whereas reduced kidney function, greater albuminuria and higher finerenone dose emerged as more clinically relevant predictors. These findings suggest that baseline potassium should not be considered in isolation when evaluating eligibility for finerenone initiation; instead, treatment decisions should incorporate overall kidney disease severity and individualized clinical risk, together with appropriate potassium monitoring. Also, our findings support the cautious initiation of finerenone in carefully selected patients with borderline or mildly elevated baseline potassium levels, provided that structured potassium monitoring and appropriate mitigation strategies are available. Future prospective studies with standardized monitoring protocols and longer follow-up are required to validate these observations and further refine individualized risk stratification.

Author Contributions: Conceptualization: M.Ö., S.Y., A.T.G., S.A., F.A., M.S., B.Ö., E.Y.A., B.D. (Betül Doğanterkin), İ.A., S.M.D., M.D. (Mustafa Demir), S.K. (Sümeysra Koyuncu), Ü.Y., A.İ. (Ayça İnci), H.Ç. (Hülya Çolak), B.D. (Bülent Demirelli), S.T., E.G.O., M.D.A., E.A. (Ezgi Avanaz), F.Y., B.D. (Beyza Doğan), S.K. (Süleyman Karaköse), M.Ş.K., B.G.D., K.T., İ.B., M.B., M.M. (Mehmet Mert), E.A. (Emre Aydın), F.Y.A., E.P., P.Ö., B.E., Z.A., M.E.D., S.S., S.Ü., Ö.B., B.A., A.A., M.İ., S.Y.K., M.M. (Meral Mert), B.D. (Belda Dursun), N.E., S.B.D., M.A.B., A.E. (Arda Erdut), G.K., M.H., A.Z.Ş., M.T., M.D. (Murat Duranay), S.F.Y., H.M.Y.U., M.A. (Murat Altunok), R.S., F.S., D.T., S.K. (Serdar Kahvecioğlu), A.S.K., T.A., H.Ç. (Hüseyin Çelik), S.K. (Sinan Kazan), İ.Ö., M.P., M.F.A., M.M. (Meral Meşe), A.D., Ü.D., E.A. (Eda Altun), S.B., E.K., C.A., M.B.A., A.İ. (Ali İlter), A.E. (Ahmet Ekmekci), S.U., M.A. (Mustafa Arıcı), E.Ş., E.A.B.; Data curation: M.Ö., A.T.G.; Formal analysis: M.Ö., A.T.G.; Investigation: M.Ö., S.Y., A.T.G., S.A., F.A., M.S., B.Ö., E.Y.A., B.D. (Betül Doğanterkin), İ.A., S.M.D., M.D. (Mustafa Demir), S.K. (Sümeysra Koyuncu), Ü.Y., A.İ. (Ayça İnci), H.Ç. (Hülya Çolak), B.D. (Bülent Demirelli), S.T., E.G.O., M.D.A., E.A. (Ezgi Avanaz), F.Y., B.D. (Beyza Doğan), S.K. (Süleyman Karaköse), M.Ş.K., B.G.D., K.T., İ.B., M.B., M.M. (Mehmet Mert), E.A. (Emre Aydın), F.Y.A., E.P., P.Ö., B.E., Z.A., M.E.D., S.S., S.Ü., Ö.B., B.A., A.A., M.İ., S.Y.K., M.M. (Meral Mert), B.D. (Belda Dursun), N.E., S.B.D., M.A.B., A.E. (Arda Erdut), G.K., M.H., A.Z.Ş., M.T., M.D. (Murat Duranay), S.F.Y., H.M.Y.U., M.A. (Murat Altunok), R.S., F.S., D.T., S.K. (Serdar Kahvecioğlu), A.S.K., T.A., H.Ç. (Hüseyin Çelik), S.K. (Sinan Kazan), İ.Ö., M.P., M.F.A., M.M. (Meral Meşe), A.D., Ü.D., E.A. (Eda Altun), S.B., E.K., C.A., M.B.A., A.İ. (Ali İlter), A.E. (Ahmet Ekmekci), S.U., M.A. (Mustafa Arıcı), E.Ş., E.A.B.; Methodology: M.Ö., S.Y., A.T.G., E.A.B.; Project administration: M.Ö., S.Y., A.T.G., E.A.B.; Resources: M.Ö., S.Y., A.T.G., S.A., F.A., M.S., B.Ö., E.Y.A., B.D. (Betül Doğanterkin), İ.A., S.M.D., M.D. (Mustafa Demir), S.K. (Sümeysra Koyuncu), Ü.Y., A.İ. (Ayça İnci), H.Ç. (Hülya Çolak), B.D. (Bülent Demirelli), S.T., E.G.O., M.D.A., E.A. (Ezgi Avanaz), F.Y., B.D. (Beyza Doğan), S.K. (Süleyman Karaköse), M.Ş.K., B.G.D., K.T., İ.B., M.B., M.M. (Mehmet Mert), E.A. (Emre Aydın), F.Y.A., E.P., P.Ö., B.E., Z.A., M.E.D., S.S., S.Ü., Ö.B., B.A., A.A., M.İ., S.Y.K., M.M. (Meral Mert), B.D. (Belda Dursun), N.E., S.B.D., M.A.B., A.E. (Arda Erdut), G.K., M.H., A.Z.Ş., M.T., M.D. (Murat Duranay), S.F.Y., H.M.Y.U., M.A. (Murat Altunok), R.S., F.S., D.T., S.K. (Serdar Kahvecioğlu), A.S.K., T.A., H.Ç. (Hüseyin Çelik), S.K. (Sinan Kazan), İ.Ö., M.P., M.F.A., M.M. (Meral Meşe), A.D., Ü.D., E.A. (Eda Altun), S.B., E.K., C.A., M.B.A., A.İ. (Ali İlter), A.E. (Ahmet Ekmekci), S.U., M.A. (Mustafa Arıcı), E.Ş., E.A.B.; Software: M.Ö., A.T.G.; Supervision: M.Ö., S.Y., A.T.G., E.A.B.; Validation: M.Ö., S.Y., A.T.G., E.A.B.; Visualization: M.Ö., A.T.G.; Writing—original draft: M.Ö., S.Y., A.T.G., E.A.B.; Writing—review and editing: M.Ö., S.Y., A.T.G., S.A., F.A., M.S., B.Ö., E.Y.A., B.D. (Betül Doğanterkin), İ.A., S.M.D., M.D. (Mustafa Demir), S.K. (Sümeysra Koyuncu), Ü.Y., A.İ. (Ayça İnci), H.Ç. (Hülya Çolak), B.D. (Bülent Demirelli), S.T., E.G.O., M.D.A., E.A. (Ezgi Avanaz), F.Y., B.D. (Beyza Doğan), S.K. (Süleyman Karaköse), M.Ş.K., B.G.D., K.T., İ.B., M.B., M.M. (Mehmet Mert), E.A. (Emre Aydın), F.Y.A., E.P., P.Ö., B.E., Z.A., M.E.D., S.S., S.Ü., Ö.B., B.A., A.A., M.İ., S.Y.K., M.M. (Meral Mert), B.D. (Belda Dursun), N.E., S.B.D., M.A.B., A.E. (Arda Erdut), G.K., M.H., A.Z.Ş., M.T., M.D. (Murat Duranay), S.F.Y., H.M.Y.U., M.A. (Murat Altunok), R.S., F.S., D.T., S.K. (Serdar Kahvecioğlu), A.S.K., T.A., H.Ç. (Hüseyin Çelik), S.K. (Sinan Kazan), İ.Ö., M.P., M.F.A., M.M. (Meral Meşe), A.D., Ü.D., E.A. (Eda Altun), S.B., E.K., C.A., M.B.A., A.İ. (Ali İlter), A.E. (Ahmet Ekmekci), S.U., M.A. (Mustafa Arıcı), E.Ş., E.A.B.

S.U., M.A. (Mustafa Arıcı), E.Ş., E.A.B. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Patients in the study were assigned an anonymous identification number for confidentiality. The study complies with the principles outlined in the Declaration of Helsinki, and it was approved by the Kartal Dr. Lütfi Kırdar City Hospital Ethical Board on 25 December 2024, decision number: 2024/010.99/11/23, and each participating center also provided institutional approval.

Informed Consent Statement: Due to the retrospective and non-interventional nature of the study, informed consent was waived.

Data Availability Statement: SPSS outputs are uploaded in a data repository and are freely available at <https://doi.org/10.6084/m9.figshare.32114377>. Raw data are available upon reasonable request.

Conflicts of Interest: Alper Tuna Guven reports a relationship with Bayer Turkey that includes speaking and lecture fees. The other authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

1. Genitsaridi, I.; Salpea, P.; Salim, A.; Sajjadi, S.F.; Tomic, D.; James, S.; Thirunavukkarasu, S.; Issaka, A.; Chen, L.; Basit, A.; et al. 11th edition of the IDF Diabetes Atlas: Global, regional, and national diabetes prevalence estimates for 2024 and projections for 2050. *Lancet Diabetes Endocrinol.* **2026**, *14*, 149–156. [CrossRef] [PubMed]
2. Ndumele, C.E.; Rangaswami, J.; Chow, S.L.; Neeland, I.J.; Tuttle, K.R.; Khan, S.S.; Coresh, J.; Mathew, R.O.; Baker-Smith, C.M.; Carnethon, M.R.; et al. Cardiovascular-Kidney-Metabolic Health: A Presidential Advisory From the American Heart Association. *Circulation* **2023**, *148*, 1606–1635. [CrossRef] [PubMed]
3. Thomas, M.C. The clustering of Cardiovascular, Renal, Adipo-Metabolic Eye and Liver disease with type 2 diabetes. *Metabolism* **2022**, *128*, 154961. [CrossRef] [PubMed]
4. Romeo, S.; Vidal-Puig, A.; Husain, M.; Ahima, R.; Arca, M.; Bhatt, D.L.; Diehl, A.M.; Fontana, L.; Foo, R.; Frühbeck, G.; et al. Clinical staging to guide management of metabolic disorders and their sequelae: A European Atherosclerosis Society consensus statement. *Eur. Heart J.* **2025**, *46*, 3685–3713. [CrossRef] [PubMed]
5. Yang, X.C.; Shao, L.L.; Mi, Y.J.; Zhang, W.H.; Liu, N.Y.; Liu, R.B.; Zhou, X.-X.; Zhang, W.-H.; Tian, Q.-B. Effect of renin-angiotensin-aldosterone system inhibitors on all-cause mortality and major cardiovascular events in patients with diabetes: A meta-analysis focusing on the number needed to treat and minimal clinical effect. *J. Diabetes Complicat.* **2021**, *35*, 107830. [CrossRef] [PubMed]
6. Malek, V.; Suryavanshi, S.V.; Sharma, N.; Kulkarni, Y.A.; Mulay, S.R.; Gaikwad, A.B. Potential of Renin-Angiotensin-Aldosterone System Modulations in Diabetic Kidney Disease: Old Players to New Hope! *Rev. Physiol. Biochem. Pharmacol.* **2021**, *179*, 31–71. [CrossRef] [PubMed]
7. Naaman, S.C.; Bakris, G.L. Diabetic Nephropathy: Update on Pillars of Therapy Slowing Progression. *Diabetes Care* **2023**, *46*, 1574–1586. [CrossRef] [PubMed]
8. McGuire, D.K.; Shih, W.J.; Cosentino, F.; Charbonnel, B.; Cherney, D.Z.I.; Dagogo-Jack, S.; Pratley, R.; Greenberg, M.; Wang, S.; Huyck, S.; et al. Association of SGLT2 Inhibitors With Cardiovascular and Kidney Outcomes in Patients With Type 2 Diabetes: A Meta-analysis. *JAMA Cardiol.* **2021**, *6*, 148–158. [CrossRef] [PubMed]
9. Zelniker, T.A.; Wiviott, S.D.; Raz, I.; Im, K.; Goodrich, E.L.; Bonaca, M.P.; Mosenzon, O.; Kato, E.; Cahn, A.; Furtado, R.H.M.; et al. SGLT2 inhibitors for primary and secondary prevention of cardiovascular and renal outcomes in type 2 diabetes: A systematic review and meta-analysis of cardiovascular outcome trials. *Lancet* **2019**, *393*, 31–39. Erratum in *Lancet* **2019**, *393*, 30. [https://doi.org/10.1016/S0140-6736\(18\)33206-9](https://doi.org/10.1016/S0140-6736(18)33206-9). [CrossRef] [PubMed]
10. Alicic, R.Z.; Rooney, M.T.; Tuttle, K.R. Diabetic Kidney Disease. *Clin. J. Am. Soc. Nephrol.* **2017**, *12*, 2032–2045. [CrossRef] [PubMed]
11. Savarese, G.; Lindberg, F.; Filippatos, G.; Butler, J.; Anker, S.D. Mineralocorticoid receptor overactivation: Targeting systemic impact with non-steroidal mineralocorticoid receptor antagonists. *Diabetologia* **2024**, *67*, 246–262. [CrossRef] [PubMed]
12. Pitt, B.; Filippatos, G.; Agarwal, R.; Anker, S.D.; Bakris, G.L.; Rossing, P.; Joseph, A.; Kolkhof, P.; Nowack, C.; Schloemer, P.; et al. Cardiovascular Events with Finerenone in Kidney Disease and Type 2 Diabetes. *N. Engl. J. Med.* **2021**, *385*, 2252–2263. [CrossRef] [PubMed]

13. Bakris, G.L.; Agarwal, R.; Anker, S.D.; Pitt, B.; Ruilope, L.M.; Rossing, P.; Kolkhof, P.; Nowack, C.; Schloemer, P.; Joseph, A.; et al. Effect of Finerenone on Chronic Kidney Disease Outcomes in Type 2 Diabetes. *N. Engl. J. Med.* **2020**, *383*, 2219–2229. [[CrossRef](#)] [[PubMed](#)]
14. Agarwal, R.; Joseph, A.; Anker, S.D.; Filippatos, G.; Rossing, P.; Ruilope, L.M.; Pitt, B.; Kolkhof, P.; Scott, C.; Lawatscheck, R.; et al. Hyperkalemia Risk with Finerenone: Results from the FIDELIO-DKD Trial. *J. Am. Soc. Nephrol.* **2022**, *33*, 225–237. [[CrossRef](#)] [[PubMed](#)]
15. Idowu, A.; Bryan Lo, K.; Adebolu, O.; Hamilton, M.; Abdelmaseeh, P.; Navaneethan, S.D.; Rangaswami, J. Hyperkalemia risk of finerenone versus spironolactone in CKD patients with type 2 diabetes. *Nephrol. Dial. Transplant.* **2025**, *40*, 1996–1999. [[CrossRef](#)] [[PubMed](#)]
16. Kerendia Product Information. European Medicines Agency [Internet]. Kerendia Product Information. 2026. Available online: <https://www.ema.europa.eu/en/medicines/human/EPAR/kerendia#product-info> (accessed on 30 April 2026).
17. Özdede, M.; Yadigar, S.; Güven, A.T.; Akgür, S.; Arslan, F.; Sezen, M.; Özcan, B.; Ayaz, E.Y.; Doğanterkin, B.; Atay, I.; et al. Hyperkalemia Risk with Finerenone in Diabetic Kidney Disease: A Real-World Analysis from the FINE-TURK Cohort. *Preprints* **2026**. [[CrossRef](#)]
18. Yadigar, S.; Akgür, S.; Arslan, F.; Sezen, M.; Özcan, B.; Ayaz, E.Y.; Doğanterkin, B.; Atay, I.; Değer, S.M.; Demir, M.; et al. Real-World Effects of Finerenone in Diabetics Kidney Disease: Data from Fine-Turk Study (Preprint) [Internet]. 2026. Available online: <https://www.researchsquare.com/article/rs-9043582/v1> (accessed on 18 March 2026).
19. Agarwal, R.; Green, J.B.; Heerspink, H.J.L.; Mann, J.F.E.; McGill, J.B.; Mottl, A.K.; Rosenstock, J.; Rossing, P.; Vaduganathan, M.; Brinker, M.; et al. Finerenone with Empagliflozin in Chronic Kidney Disease and Type 2 Diabetes. *N. Engl. J. Med.* **2025**, *393*, 533–543. [[CrossRef](#)] [[PubMed](#)]
20. Kovesdy, C.P.; Ebert, N.; Vizcaya, D.; Walsh, M.; Kosiborod, M.N.; Layton, J.B.; Ziemiecki, R.; Johannes, C.B.; Pladevall-Vila, M.; Gee, P.O.; et al. Change in Urine Albumin-Creatinine Ratio and Occurrence of Hyperkalemia in Patients Initiating Finerenone in the USA: A Cohort Study from the FOUNTAIN Platform. *Nephron* **2025**, *149*, 371–383. [[CrossRef](#)] [[PubMed](#)]
21. Wheeler, D.C.; Pantalone, K.M.; Guo, L.; Desai, N.R.; Correa-Rotter, R.; Nicholas, S.B.; Kim, N.H.; Zheng, Z.; Scott, C.; Horvat-Broecker, A.; et al. Dosing, treatment patterns and safety of finerenone use in routine care: An interim analysis of the prospective, real-world and observational FINE-REAL study. *Clin. Kidney J.* **2025**, *18*, sfaf305. [[CrossRef](#)] [[PubMed](#)]
22. Stevens, P.E.; Ahmed, S.B.; Carrero, J.J.; Foster, B.; Francis, A.; Hall, R.K.; Herrington, W.G.; Hill, G.; Inker, L.A.; Kazancioğlu, R.; et al. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int.* **2024**, *105*, S117–S314. [[CrossRef](#)] [[PubMed](#)]
23. Ceasovschih, A.; Şorodoc, V.; Covantsev, S.; Balta, A.; Uzokov, J.; Kaiser, S.E.; Almaghraby, A.; Lionte, C.; Stătescu, C.; Sascău, R.; et al. Electrocardiogram Features in Non-Cardiac Diseases: From Mechanisms to Practical Aspects. *J. Multidiscip. Healthc.* **2024**, *17*, 1695–1719. [[CrossRef](#)] [[PubMed](#)]

Disclaimer/Publisher’s Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.