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Prevalence and Management of Cardio Kidney Metabolic Disease (CKM) in the Middle East

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Introduction

The Cardiovascular-Kidney-Metabolic (CKM) syndrome has emerged as a critical determinant of premature morbidity and mortality. For better understanding and management, five stages have been identified based on CKM risk factors [1].

Diabetes plays a pivotal role in CKM, often leading to Diabetic Kidney Disease (DKD), End-Stage Renal Disease (ESRD), and cardiovascular (CV) complications [2,3]. Patients with diabetes are vulnerable to Heart Failure (HF), including Reduced Ejection Fraction (HFrEF) or HF with Preserved Ejection Fraction (HFpEF) [4]. Chronic Kidney Disease (CKD) severity is typically assessed using Kidney Disease Improving Global Outcomes (KDIGO) guideline, which considers estimated Glomerular Filtration Rate (eGFR) and Albumin Creatinine Ratio or albuminuria (ACR) [5]. Albuminuria is an established biomarker for CKD and a predictor of cardiovascular disease (CVD) associated risk [6]. Additional biomarkers include C-Reactive Protein (CRP), B-type Natriuretic Peptide (BNP), and N-terminal pro-B-type Natriuretic Peptide (NT pro-BNP) tests for early diagnosis of CVD and HF [6-8].

Several studies highlight global prevalence of CKM [9,10]. In the Gulf Cooperation Council (GCC) countries, Type 2 Diabetes (T2D) prevalence ranges between 7.2-11.3%, exceeding global prevalence of 8.8% and expected to increase by 96.3% by 2035 [11,12]. Additionally, this region has also exhibited a high prevalence of HF [13,14].

Management strategies of CKM include Sodium-Glucose Cotransporter 2 (SGLT2) inhibitors, Renin-Angiotensin-System Inhibitors (RASi), Glucagon-like Peptide-1 Receptor Agonists (GLP-1RAs), and nonsteroidal mineralocorticoid receptor antagonist, finerenone [1,15-18]. Finerenone, a selective nonsteroidal MRA, has demonstrated promising benefits on CV health in patients with CKD and T2D [18,19]. Guidelines recommend finerenone with RASi or SGLT2 inhibitors in high or very high-risk patients, as it reduces CKD progression and CVD, saving societal costs [20]. However, the usage of finerenone remains limited due to hyperkalemia risk, patient-based treatment nonadherence and inadequate follow-up [21].

This paper highlights finerenone usage in the Middle East, based on a virtual expert meeting. The objective of the meeting was to achieve expert consensus concerning several critical questions regarding finerenone, which included optimal timing for treatment initiation, compatibility with RASi, effectiveness in T2D patients irrespective of their eGFR levels, and managing T2D-associated HF. Additionally, the meeting also addressed potassium monitoring timelines and barriers to finerenone adoption.

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Description

On October 12, 2024, a meeting convened five Key Opinion Leaders (KOLs) from UAE, Saudi Arabia, and Kuwait, comprising cardiologists and nephrologists recognized as experts and active researchers. The meeting highlighted literature on CKM guidelines, prevalence, treatment, and barriers to finerenone adoption, followed by sharing insights on crucial questions by KOLs.

The panel extensively discussed the prevalence of CKM across these countries and agreed that diabetic patients are at high risk of developing CKM. The panel members concurred that initiating finerenone treatment during early stages can act on inflammation, thereby reducing cardiorenal risk. They also emphasized early and effective utilization of finerenone in managing CV conditions. The panel unanimously accepted the use of finerenone in addition to SGLT2 and RASi as recommended in guidelines [1,5,15,16] and also agreed that the treatments of SGLT2 inhibitors, RASi, and finerenone are additive. They emphasized the sequential/spacing addition of these three drugs for optimal benefits. The follow-ups are recommended every four weeks, and all three therapies should be introduced over the period of 12 weeks or three months. However, as per the panel members, finerenone should not be recommended to nonproteinuric T2D patients, as ongoing trials are evaluating its efficacy in nonproteinuric DKD.

Further, the panel discussed the utility of these treatments in patients with low Blood Pressure (BP). The experts agreed that the RASi could not be recommended for patients with low BP [16,22]. The experts unanimously suggested the use of finerenone along with SGLT2 in patients with low BP and proteinuria.

An emerging concern was raised by the panel on the elevated risk of CKM among the younger population, attributed to several factors such as obesity, sleep apnea, and prediabetes. Further, they highlighted that diagnosis occurs only after the manifestation of symptoms, thereby emphasizing the need for timely interventions. Therefore, to enhance early detection, the panel members recommended annual check-ups for GFR, ACR, and proBNP tests, as well as biannual assessments for key risk factors like Hb1Ac and LDL. For patients with higher LDL levels, they recommended check-ups every four to six weeks to ensure timely management.

As per the KDIGO guidelines, finerenone is recommended in patients with GFR>25 mL/min/1.73 m^2 and should not be prescribed when GFR<25mL/min/1.73 m^2 [5]. All the panel members agreed to this administration of finerenone as per KDIGO guidelines. Further, the panel also highlighted the criticality of ACR as a sensitive marker of CV disease. However, they highlighted the inconsistency of units to measure ACR across hospitals or centers, causing confusion in determining the albuminuria stage. The panel strongly recommended standardizing measurement practices to ensure clarity and accuracy. They also stressed that early detection of albuminuria, diabetes, and other related risk factors is vital for effective CKM management. Additionally, primary healthcare providers were identified as pivotal in initiating timely interventions to control the progression of CKM.

The treatment of finerenone carries a potential risk of hyperkalemia, especially at the later stages of CKD. The experts emphasized the importance of potassium binders in managing elevated potassium levels. They insisted on not prescribing finerenone if potassium levels exceeded 4.8. In such instances, they recommend stabilizing potassium levels before initiating finerenone treatment. They recommended regular potassium level monitoring in these patients (once every 2-4 weeks).

According to experts, primary health care providers and General Practitioners (GPs) have become increasingly knowledgeable about the treatment options, except for a few in the UAE. These providers play a pivotal role in managing diabetic patients and initiating appropriate treatment before referring them to nephrologists or cardiologists. However, the infrastructure and instruments required for related pathological tests are unavailable in many polyclinics.

The meeting further insisted on the importance of patient awareness, stressing the need to encourage regular check-ups and medication refills. Lack of regular check-ups poses challenges in checking potassium and GFR levels. Experts highlighted that drug treatment in the GCC region runs smoothly with the insurance companies at both private and government hospitals; however, in some regions, practitioners face unavailability of drugs at government hospitals and issues with the insurance companies at private hospitals. To address these challenges, the panel suggested the engagement of GPs, stakeholders, insurance companies, and the government to promote this organ-protective medication and expand the prescribing authority for finerenone beyond nephrologists and cardiologists to include endocrinologists and GPs.

Recently, the FINEARTS-HF Phase III trial evaluated the long-term efficacy and safety of finerenone with HFmrEF and HFpEF. Finerenone was shown to reduce worsening of HF by 18% in total and by 16% in patients with HFmrEF and HFpEF at its primary endpoint [23,24].

Conclusion

Key takeaways from the meeting:

1. Early use of finerenone aids managing CV conditions.

2. Sequential/spacing addition of finerenone to SGLT2 and RASi treatments was recommended to avoid any initial dipping of eGFR (approximately 4-6 weeks).

3. Finerenone may be beneficial in T2D patients with associated CKD. Moreover, this drug also suits low BP patients and doesn't have any further restrictions on HbA1C levels.

4. Regular checkups: annually for GFR, ACR, pro-BNP; biannual for HbA1c, LDL.

5. Hyperkalemia is manageable with regular potassium monitoring.

6. The panel emphasized involving GPs, insurance companies, governments, and stakeholders to streamline finerenone administration in GCC countries.

7. More GCC studies recommended assessing CKM prevalence.

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Conflict of Interest

No conflict of interest.

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