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Review Article

Finerenone in Diabetic-Kidney Disease, Renal and Cardiovascular Outcome: A Meta-Analysis of Independent Trial Registries

Felicita Gracia[1], Arya Marganda Simanjuntak[2], Samira Amanda[3], Linda Ida Mustika[1], Juwanto[2], Ligat Pribadi Sembiring[2], Jazil Karimi[2], Sari Harahap[2], Rosmaliana[4]

[1]Faculty of Medicine and Health Sciences, Universitas Bangka Belitung, Pangkal Pinang, Indonesia
[2]Department of Internal Medicine, Faculty of Medicine, Universitas Riau, Arifin Achmad General Hospital, Pekanbaru, Indonesia
[3]Faculty of Medicine, Universitas Riau, Pekanbaru, Indonesia
[4]Department of Cardiovascular, Faculty of Medicine, Universitas Riau, Arifin Achmad General Hospital, Pekanbaru, Indonesia

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Corresponding Author:
Felicita Gracia, Faculty of Medicine and Health Sciences, Universitas Bangka Belitung, Pangkalpinang, Bangka Belitung, Indonesia,
felicitagracia0905@gmail.com

ABSTRACT

Background: Diabetic kidney disease (DKD) remains a frequent complication of type 2 diabetes, which significantly increases cardiovascular risk. Despite existing treatments, a substantial risk of disease progression still remains, leading to further exploration in Finerenone, a selective nonsteroidal mineralocorticoid receptor antagonist.

Objective: This meta-analysis evaluates finerenone's effects on the improvement of cardiorenal outcomes in DKD.

Methods: A Systematic Review and Meta-Analysis (PROSPERO CRD420251122382) followed PRISMA guidelines. PubMed, ScienceDirect, and Epistemonikos utilized and used keywords "Finerenone AND Diabetes AND Chronic Kidney Disease AND Outcomes." RCTs comparing finerenone to placebo in DKD, reporting renal or cardiovascular outcomes, were included. Data extraction covered study characteristics and outcomes. RevMan 5.4 analyzed data using a random-effects model. Risk of bias (RoB2) and certainty of evidence (GRADE-PRO) were assessed.

Results: Three RCTs (19,027 participants) were included for renal outcomes, and two RCTs (13,026 participants) for cardiovascular outcomes. Finerenone significantly reduced the odds of sustained eGFR decline ≥40% (OR 0.83, p=0.0003) and≥57% (OR 0.86, p=0.0001), as well as the major composite kidney outcome (OR 0.76, p<0.0001). ESKD odds reduction (21%) was not statistically significant. For cardiovascular outcomes, finerenone significantly reduced hospitalization for heart failure (OR 0.78, p=0.0001). Trends towards reduced cardiovascular death (OR 0.88, p=0.09) were noted. Studies had low bias risk, and most outcomes showed moderate evidence certainty.

Conclusions: Finerenone is associated with significant renoprotection and significantly reduces heart failure hospitalizations in DKD. Finerenone as an effective nonsteroidal mineralocorticoid receptor antagonist for comprehensive management, improving cardiorenal outcomes in this high-risk group.

Keywords: Chronic kidney disease, cardiovascular, diabetes, finerenone, renal.

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Introduction

Currently, global health data shows approximately 589 million adults affected by diabetes, representing 11.1% of the world's population. Projections suggest figures will climb up to 853 million by 2050, with Type 2 Diabetes Mellitus (T2DM) constituting 90% of the cases.[1–3] A critical yet frequent complication of T2DM is diabetic kidney disease (DKD), impacting 20-50% of T2DM patients, and DKD itself remains the primary driver of chronic kidney disease (CKD) and end-stage kidney disease (ESKD).[4] While International guidelines emphasize management of CKD in T2DM patients through control of hypertension and hyperglycemia using renin-angiotensin system (RAS) blockers and sodium-glucose cotransporter 2 (SGLT2) inhibitors, the risk of CKD progression remains significant, leading to a need for the development of newer therapies.[5–7]

Finerenone emerged as one of the potent nonsteroidal MRAs (mineralocorticoid receptor antagonists) with high selectivity for MR (mineralocorticoid receptor). Compared to steroidal MRAs, finerenone possesses a shorter half-life, no active metabolites, demonstrating higher selectivity to MR compared to spironolactone and enhanced receptor binding affinity to eplerenone.[8,9] Clinical studies have also assessed Finerenone in mitigating cardiorenal risks, such can be seen in FIDELIO-DKD and FIGARO DKD trials.[10,11] Previously, several meta-analyses have discussed the role of finerenone towards renal and cardiovascular outcomes of patients with DKD, however the inclusion of those studies includes overlapping data from the subgroup analysis derived from the same RCT registry. This methodology can result in overlapping patient populations, potentially affecting the independence of pooled data in the research. Consequently, there is a need for a meta-analysis that re-analyses the data according to the RCT registry to provide an analysis of independent primary trial results without any data duplication to provide a clear synthesis of independent data points.

Methods

Protocol registration

Protocols employed in this study have been registered and accepted by PROSPERO, with the identification number [CRD420251122382]. This systematic review and meta-analysis were prepared in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[12]

Search strategy

Various search engines to search for articles including PubMed, ScienceDirect, and Epistemonikos. Each author independently screened each database, extracting references manually and using Zotero's Reference Manager for duplicate reduction. "Finerenone AND Diabetes AND Chronic Kidney Disease AND Outcomes" served as the basis for our keyword selection.

Eligibility criteria

The eligibility criteria for this study were based on the PICOS framework, with additional inclusion and exclusion criteria. PICOS framework comprises the following elements: [P]atients, Diabetic Kidney Disease patient; [I]ntervention, Finerenone; [C]omparator, Control OR Placebo; [O]utcome, Cardiovascular Outcome and Renal Outcome, and [S]tudy, Randomized Controlled Trial (RCT). Inclusion criteria are: (1) article in Indonesia or English, and (2) Full-Text available. Review articles, animal studies, editorials, commentaries, and non-accessible articles were excluded.

Data extraction and statistical analysis

Various data extracted from included studies such as: (1) First author name, (2) Year of Publication, (3) RCT registry, (4) RCT code name, (5) number of sample, (6) Age, (7) Gender, (8) intervention description, (9) duration of follow up, (10) Renal outcome, such as eGFR kidney composite, ESKD event and (11) Cardiovascular outcome, such as time to CV death, Non-Fatal Myocardial Infarction, Non-Fatal Stroke, Hospitalization of Heart Failure. RevMan 5.4 was utilized for statistical meta-analysis of a dichotomous outcome. Randomized

Effect Model (REM) was used to generalize the result so it is not limited to inclusion alone. Heterogeneity was analyzed by the I2 value.

Risk of bias and quality assessment

We analyzed the risk of bias for our RCTs using RoB2 by assessing study quality based on the five domains in RoB2. The assessment was done with the conclusion of Low Risk / Some Concern / High Risk. Conclusions were presented using a summary plot and a traffic plot. Quality assessment for the result will be assessed with GRADE-PRO Analysis.

Result

Study selection & characteristics

We identified 906 studies across databases, and 26 of them were excluded due to duplication. We summarize our literature searching and selection in Figure 1. In the end, we include 3 articles in this review. We compile characteristics of included studies in Table 1. We include 19.027 participants, 9522 of them with the Finerenone group and 9505 Placebo. The average age of participants was relatively high, but there were no differences between the two groups in each inclusion study. No gender imbalance was observed between studies. Patients were given Finerenone orally at a dose of 10 mg or 20 mg once daily. Each study had a different follow-up period, ranging from 2.6 years to 3.4 years of observation.

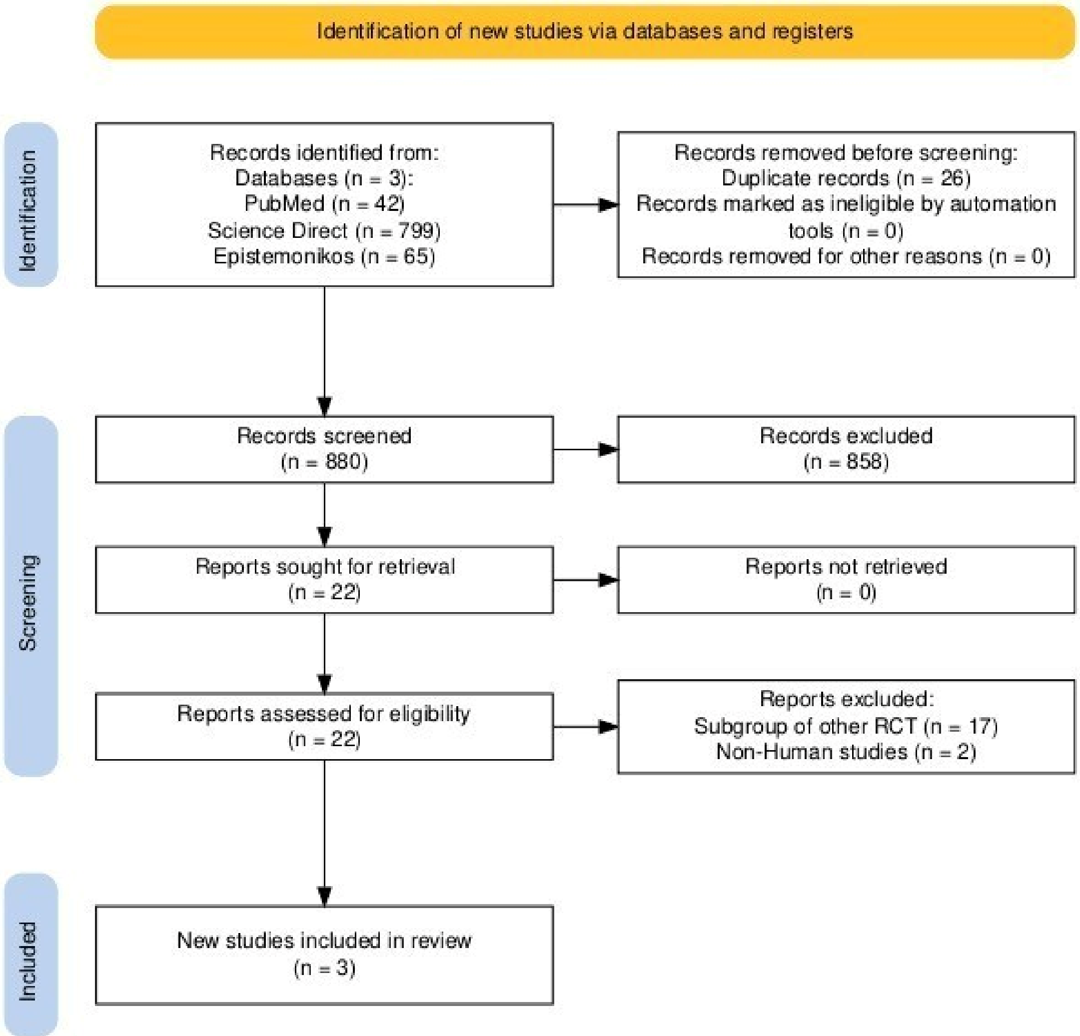

Figure 1. PRISMA FlowChart

Table 1. Characteristics of Included Studies

No	Author	Age (Finerenone)	Age (Control)	Gender (Finerenone)	Gender (Control)	Dose (Finerenone)	Follow-Up
1	Bakris et al.,[10] 2020	65.4 ± 8.9	65.7 ± 9.2	Male (1953)	Male (2030)	10 mg/ 20mg	2.6 years
2	Pitt et al.,[11] 2021	64.1 ± 9.7	64.1 ± 10	Male (2528)	Male (2577)	10 mg/ 20 mg	3.4 years
3	Finnian et al.,[13] 2025	71.94 ± 9.60	72.04 ± 9.69	Male (1648)	Male (1621)	10 mg, 20 mg or 40 mg	32 months

Renal outcome analysis

Finerenone treatment is linked to notable deceleration in the progression of kidney disease (Fig. 2 (upper portion)). The odds of a sustained decline in estimated glomerular filtration rate (eGFR) of ≥40% from baseline were 17% lower than that of the control group (pooled OR = 0.83; 95% CI, 0.75 to 0.92; p=0.0003). Consistent benefits were observed for a more severe decline in kidney function, defined as a sustained eGFR decrease of ≥57% from baseline (pooled OR = 0.86; 95% CI, 0.76 to 0.97; p=0.0001). The renoprotective effect was observed in the analysis of the major composite kidney outcome (including a sustained eGFR decrease of ≥57%, end-stage kidney disease, or renal death). Finerenone was associated with a highly significant 24% reduction in the odds of the composite kidney endpoint (pooled OR = 0.76; 95% CI, 0.68 to 0.85; p<0.0001). When evaluating the most severe renal outcomes, the effect of finerenone showed positive trends but did not reach statistical significance. There was no significant difference between groups for the outcome of an eGFR falling below 15 ml/min/1.73m2 (pooled OR = 0.89; 95% CI, 0.62 to 1.08; p=0.31). For the critical endpoint of end-stage kidney disease (ESKD), the analysis showed a clinically relevant 21% reduction in odds with finerenone. However, this result narrowly missed the threshold for statistical significance (pooled OR = 0.79; 95% CI, 0.62 to 1.01; p=0.06).

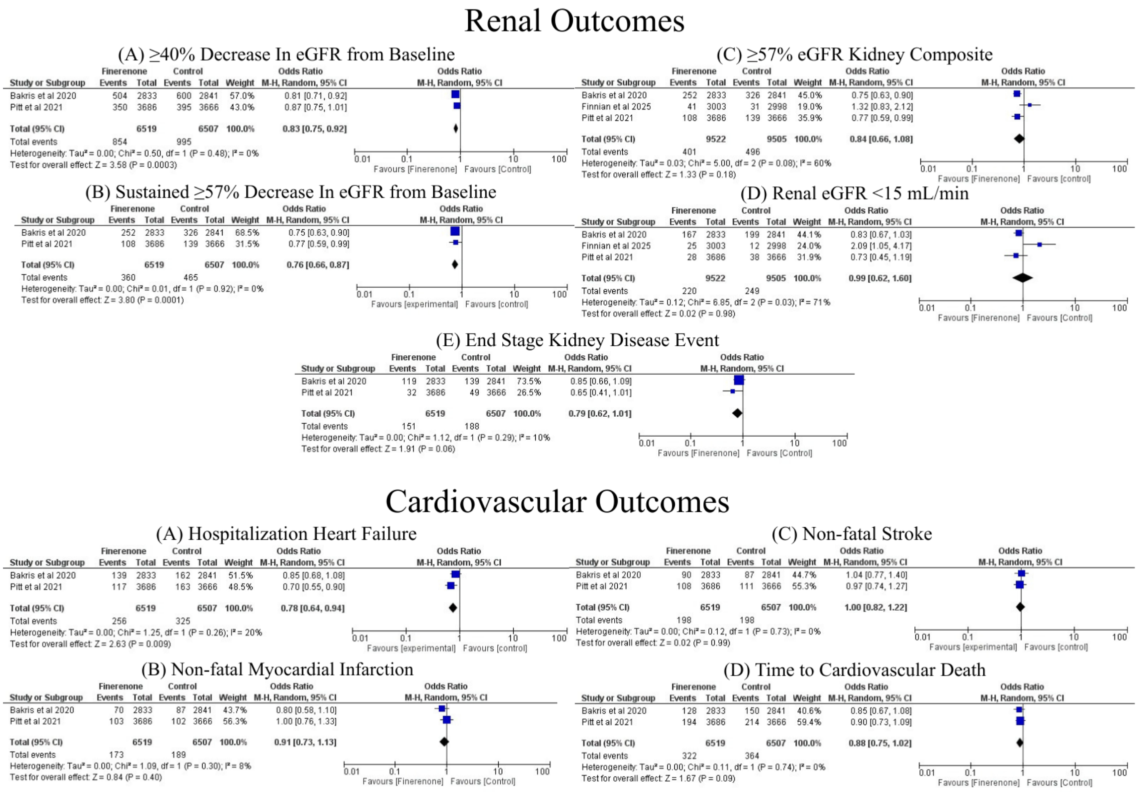

Figure 2. Forest Plot of Renal & Cardiovascular Outcome

Cardiovascular outcome analysis

We were only able to include two RCT data sets by Bakris et al and Pitt et al, which had the same cardiovascular outcome parameters and were arranged in a forest plot as shown in Fig. 2 (below renal outcome). Encompassing a total of 13,026 participants (6,519 in the finerenone arm and 6,507 in the control arm). The pooled effects of finerenone on four prespecified cardiovascular outcomes were assessed using a random-effects model. No significant statistical heterogeneity was detected across any of the analyzed outcomes (all I2=0%). Hospitalization for heart failure was lower in the finerenone group compared to placebo by 12% (OR 0.78, 95% CI: 0.64–0.94) and was statistically significant (Fig. 2A). For the endpoint of non-fatal myocardial infarction (Fig.2B), the meta-analysis found no significant difference between the intervention and control groups (pooled OR = 0.91; 95% CI, 0.73 to 1.13; p=0.40). Similarly, there was no statistically significant effect observed for the outcome of non-fatal stroke (Fig.2C). The pooled OR was 1.08 (95% CI, 0.88 to 1.32; p=0.39), indicating no discernible difference in stroke risk between the finerenone and control arms. In the analysis of cardiovascular death (Fig.2D), finerenone did not demonstrate a statistically significant reduction in odds compared to placebo (pooled OR = 0.88; 95% CI, 0.75 to 1.03). However, the result showed a strong trend towards a beneficial effect, narrowly missing statistical significance (p=0.09).

Risk of Bias

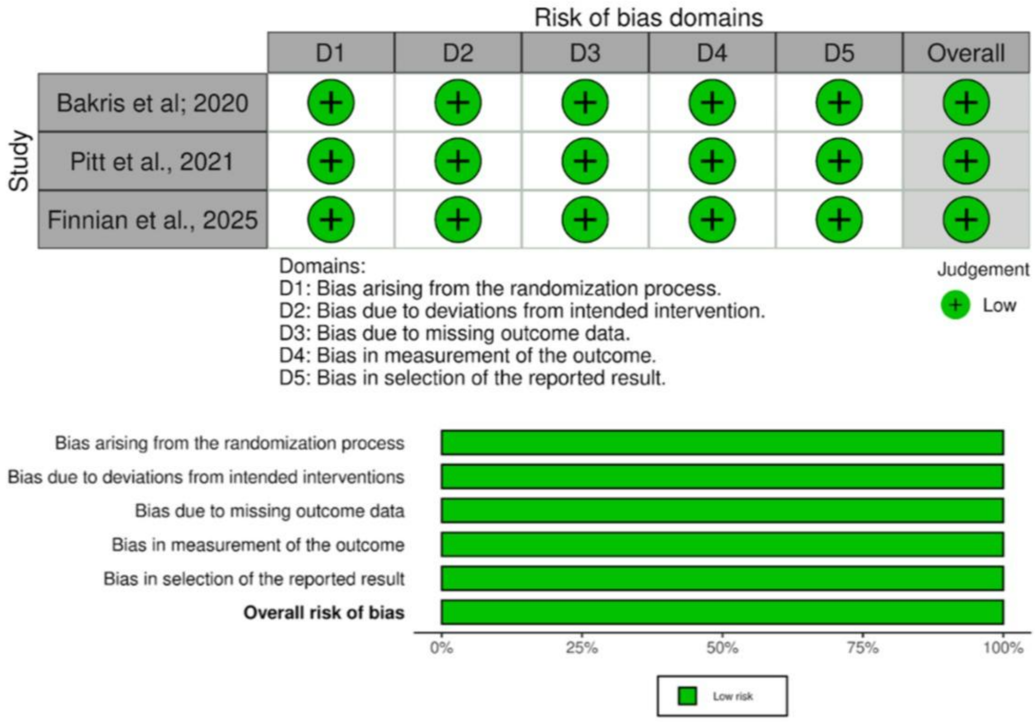

Figure 3. Traffic Light Plot & Summary Plot of Included Studies

Overall, studies have a low risk of bias and have well-conducted, large-scale randomized controlled trials with robust methodology across all domains. Studies do not indicate substantial imbalances that would suggest problems with the randomization process; there is the availability of nearly all participants' data and proper methods in measuring outcomes.

Quality assessment

Quality assessment was analyzed with GRADE-Pro for all outcomes. GRADE-PRO was compiled in Figure 4. Most of the outcomes were Moderate Certainty, except that≥57% eGFR kidney composite and Renal eGFR <15 mL/min were considered Low Certainty of evidence. It is highly likely that confidence in the results is still low despite the large sample size, as the number of studies is still relatively small, meaning there is potential for publication bias that reduces current confidence.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Finerenone	Placebo	Relative (95% CI)	Absolute (95% CI)		
Renal Outcome ≥40% Decrease in eGFR from Baseline (follow-up: range 2.4 years to 3.6 years)												
2	randomised trials	not serious	not serious	not serious	not serious	publication bias strongly suspected[a]	854/6519 (13.1%)	995/6507 (15.3%)	**OR 0.83** (0.75 to 0.92)	**23 fewer per 1,000** (from 34 fewer to 10 fewer)	⨁⨁⨁◯ Moderate[a]	
Sustained ≥57% decrease in eGFR												
2	randomised trials	not serious	not serious	not serious	not serious	publication bias strongly suspected[a]	360/6519 (5.5%)	465/6507 (7.1%)	**OR 0.76** (0.66 to 0.87)	**16 fewer per 1,000** (from 23 fewer to 9 fewer)	⨁⨁⨁◯ Moderate[a]	
≥57% eGFR kidney composite												
3	randomised trials	serious[b]	not serious	not serious	not serious	publication bias strongly suspected[a]	401/9522 (4.2%)	496/9505 (5.2%)	**OR 0.84** (0.66 to 1.08)	**8 fewer per 1,000** (from 17 fewer to 4 more)	⨁⨁◯◯ Low[a,b]	
Renal eGFR below 15 mL/min												
3	randomised trials	serious[b]	not serious	not serious	not serious	publication bias strongly suspected[a]	220/9522 (2.3%)	249/9505 (2.6%)	**OR 0.99** (0.62 to 1.60)	**0 fewer per 1,000** (from 10 fewer to 15 more)	⨁⨁◯◯ Low[a,b]	
ESKD Event												
2	randomised trials	not serious	not serious	not serious	not serious	publication bias strongly suspected[a]	151/6519 (2.3%)	188/6507 (2.9%)	**OR 0.79** (0.62 to 1.01)	**6 fewer per 1,000** (from 11 fewer to 0 fewer)	⨁⨁⨁◯ Moderate[a]	
Hospitalization Heart Failure												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Finerenone	Placebo	Relative (95% CI)	Absolute (95% CI)		
2	randomised trials	not serious	not serious	not serious	not serious	publication bias strongly suspected[a]	256/6519 (3.9%)	325/6507 (5.0%)	**OR 0.78** (0.64 to 0.94)	**11 fewer per 1,000** (from 17 fewer to 3 fewer)	⨁⨁⨁◯ Moderate[a]	
Non-fatal Myocardial Infarction												
2	randomised trials	not serious	not serious	not serious	not serious	publication bias strongly suspected[a]	173/6519 (2.7%)	189/6507 (2.9%)	**OR 0.91** (0.73 to 1.13)	**3 fewer per 1,000** (from 8 fewer to 4 more)	⨁⨁⨁◯ Moderate[a]	
Non-Fatal Stroke												
2	randomised trials	not serious	not serious	not serious	not serious	publication bias strongly suspected[a]	198/6519 (3.0%)	198/6507 (3.0%)	**OR 1.00** (0.82 to 1.22)	**0 fewer per 1,000** (from 5 fewer to 6 more)	⨁⨁⨁◯ Moderate[a]	
Cardiovascular Death												
2	randomised trials	not serious	not serious	not serious	not serious	publication bias strongly suspected[a]	322/6519 (4.9%)	364/6507 (5.6%)	**OR 0.88** (0.75 to 1.02)	**6 fewer per 1,000** (from 13 fewer to 1 more)	⨁⨁⨁◯ Moderate[a]	

CI: confidence interval; **OR**: odds ratio

Explanations

a. Only 2 RCT included

b. I2 more than 50%

Figure 4. Grade Analysis of Included Studies

Discussion

Clinical implication

This meta-analysis analyzes the clinical utility of finerenone as a therapeutic option for patients with DKD, and findings were also supported by GRADE analysis (table attached in the supplementary file). The significant reductions in key renal endpoints, particularly the major composite kidney outcome and the progression of eGFR decline, suggest that finerenone can potentially and substantially slow the rate of kidney damage in this vulnerable population. Furthermore, the significant reduction in hospitalization for heart failure highlights finerenone's additional benefit in mitigating cardiovascular complications, which are highly prevalent in DKD patients.

While the evidence for reducing ESKD or cardiovascular death did not reach conventional statistical significance, the observed positive trends are clinically meaningful and warrant consideration, especially given the established benefits for other severe renal and cardiovascular events. The findings suggest that finerenone should be considered as part of a comprehensive management strategy for patients with DKD in improving cardiorenal outcomes, thereby potentially reducing morbidity and improving quality of life. Its nonsteroidal mechanism of action and favorable safety profile (as implied by no significant heterogeneity in cardiovascular outcomes) further support its integration into clinical practice.

Limitation and strength

This study is limited by the very limited number of RCTs available, making it difficult to assess existing publication bias. This study also has not further analyzed the side effects of the treatment and the potential interactions with other medications. This is important because patients with DKD will inevitably use medications other than Finerenone, such as antidiabetic agents, antihypertensive agents, and others. There are also several parameters that have not yet reached statistical significance, which need to be further investigated to determine if there are other factors influencing these outcomes.

The strength of this study lies in the fact that, although only a few RCTs were included, the included studies were confirmed not to be duplicates of patients between RCTs. Previous meta-analyses have included studies from the same RCT registry but analyzed them further using subgroups. The issue with this data collection method in this case is the potential for data from one patient to be duplicated, appearing as if they were different patients. Thus, the strength of this study lies in prioritizing the use of non-overlapping trial registries which ensures data independence and avoids the potential for data redundancy.

Future research direction

Further RCTs are needed not only to increase the sample size, but also to compare with commonly used drug combinations in DKD patients, such as antidiabetic and antihypertensive drugs, to assess drug interactions and other potential side effects. Renal and cardiovascular parameters whose efficacy is still debated need further investigation to determine whether other factors influence the results or if the data is already accurate for general implementation. Subgroup analysis in RCTs is indeed important to identify demographic factors that may influence outcomes, however in the context of meta-analyses, it should be taken into consideration to avoid including both primary trials and their corresponding subgroup analysis simultaneously to prevent double-counting participants.

Conclusion

This meta-analysis demonstrates finerenone's renoprotective effects in diabetic kidney disease, markedly reducing kidney disease progression and major composite kidney outcomes. Additionally, it also confirms a substantial decrease in heart failure hospitalizations. While trends for ESKD and cardiovascular death were observed, the novel aspect lies in integrating comprehensive renal and cardiovascular benefits from a limited, yet highly methodologically sound, set of trials. This supports finerenone as a crucial nonsteroidal mineralocorticoid receptor antagonist for holistic management of DKD.

Declarations

Competing interests

The authors declare no conflict of interest.

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Not applicable.

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None.

Author's Contribution

Idea/concept: FG, AMS. Design: FG, AMS, SA, LIM, J, LPS, JK, SH, R. Control/supervision: FG, AMS. Data collection/processing: FG, AMS, SA, LIM, J, LPS, JK, SH, R. Analysis/interpretation: FG, AMS. Literature review: FG, AMS, SA, LIM, J, LPS, JK, SH, R. Writing the article: FG, AMS, SA, LIM, J, LPS, JK, SH, R. Critical review: FG, AMS, J, LPS, JK, SH, R. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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