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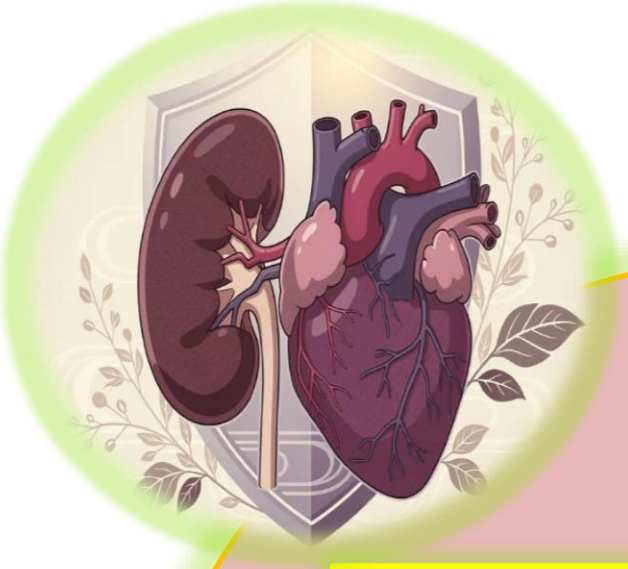


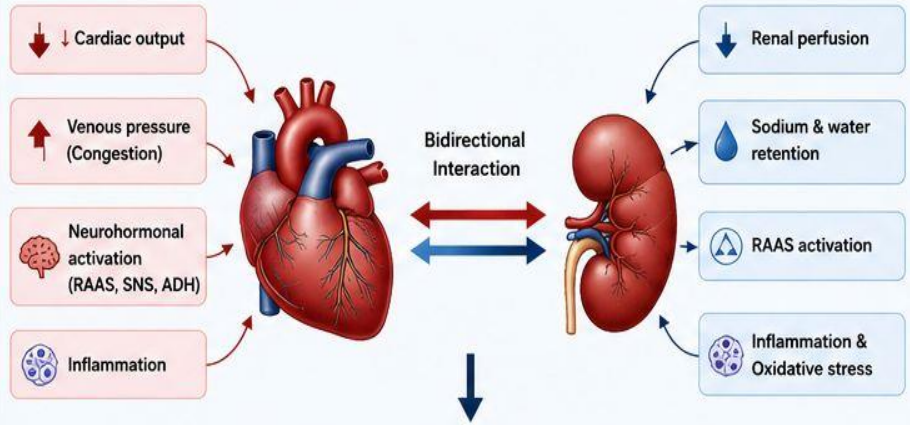
Four-Pillar Therapy In Cardiorenal Syndrome: The Expanding Role of Finerenone

Dr.Maryam Pourkar Jadid
Nephrologist(Guilan)

CARDIORENAL SYNDROME (CRS)

Traditional Concept: Interaction Between Heart and Kidney

CRS: Dysfunction of the heart or kidneys induces dysfunction of the other organ (acute or chronic)



Common Pathophysiologic Pathways

Hemodynamic alterations • Congestion • Hypoperfusion
RAAS & SNS overactivity • Inflammation • Fibrosis

Clinical Manifestations

Worsening Heart Failure • Acute Kidney Injury
Progressive Chronic Kidney Disease

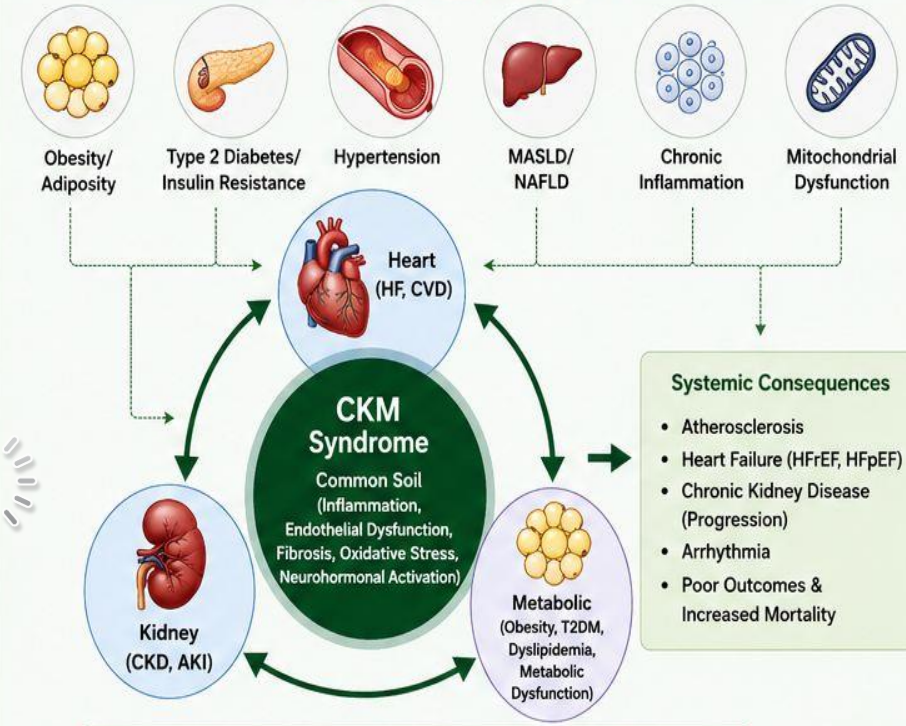
Focus: Hemodynamic and Neurohormonal Interaction

CARDIO–KIDNEY–METABOLIC SYNDROME (CKM)

Modern Concept: Systemic Interconnected Syndrome

CKM: Interconnected disorders of the heart, kidney, and metabolic systems arising from shared risk factors and pathophysiologic pathways

Shared Risk Factors and Drivers



Systemic Consequences

- Atherosclerosis
- Heart Failure (HFrEF, HFpEF)
- Chronic Kidney Disease (Progression)
- Arrhythmia
- Poor Outcomes & Increased Mortality

Focus: Shared Metabolic–Inflammatory–Fibrotic Network

THE RELATIONSHIP

CRS in the CKM Era

CRS is not an isolated entity. It is often the clinical expression of advanced CKM syndrome.

From Interaction to Interconnection

From a "two-organ" interaction model to a "systemic" model driven by metabolic–inflammatory–fibrotic pathways.

Therapeutic Implication

Treat the underlying CKM drivers to prevent, slow, or reverse cardiorenal complications.

Disease-Modifying Therapies Targeting CKM

- SGLT2 Inhibitors
- Finerenone (ns-MRA)
- GLP-1 RA / Dual GIP-GLP-1 RA
- Lifestyle: Weight, Exercise, Diet
- Optimal BP, Lipids, Glycemic Control

CKM provides the pathophysiologic framework; CRS is one of its clinical manifestations.
Treat the soil, not just the organ.

Heart Kidney Metabolic

COMMON SOIL

THE SHARED GROUND OF CARDIORENAL SYNDROME

"Not just heart damaging kidney or kidney damaging heart, but both organs growing in the same pathologic soil

THE COMPONENTS OF COMMON SOIL

TYPE 2 DIABETES
- Hyperglycemia
- Chronic inflammation
- Oxidative stress
- Fibrosis (heart & kidney)

HYPERTENSION
- Increased glomerular pressure
- Left ventricular hypertrophy
- Atherosclerosis

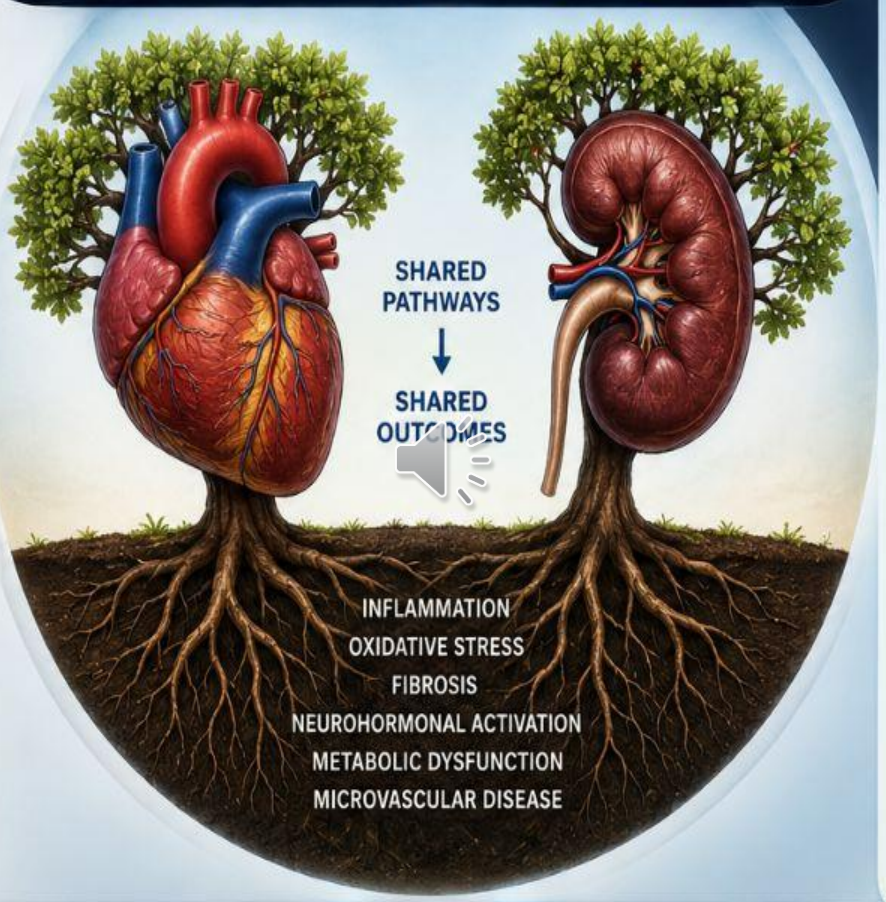
OBESITY
- Insulin resistance
- Adipose tissue inflammation
- RAAS activation

CHRONIC INFLAMMATION
- ↑ IL-6, TNF-α, CRP

OXIDATIVE STRESS
- Reactive oxygen species mediated injury

NEUROHORMONAL ACTIVATION
- RAAS activation
- Sympathetic nervous system activation

ATHEROSCLEROSIS & ENDOTHELIAL DYSFUNCTION
- Systemic vascular disease



CLINICAL IMPLICATION

Cardiorenal syndrome is not merely bi-directional injury between heart and kidney, but a consequence of a shared pathologic milieu.

THERAPEUTIC IMPLICATION

Targeting the "common soil" protects both heart and kidney

SGLT2 INHIBITORS
Empagliflozin, Dapagliflozin...

NONSTEROIDAL MRA
Finerenone

GLP-1 RECEPTOR AGONISTS
Semaglutide, Liraglutide...

RAAS INHIBITORS
ACEi / ARB / ARNI

These therapies reduce inflammation, fibrosis, oxidative stress and metabolic dysfunction, improving the common soil.

THE KEY MESSAGE

"The heart and kidney are two trees rooted in the same toxic soil."
If we treat only one tree, the disease persists; if we heal the soil, both organs recover."

INFLAMMATION | OXIDATIVE STRESS | FIBROSIS | NEUROHORMONAL ACTIVATION | METABOLIC DYSFUNCTION

ONE SOIL • TWO ORGANS • ONE STRATEGY • BETTER OUTCOMES

www.kidney-international.org

Kidney disease and heart failure: recent advances and current challenges: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference

OPEN

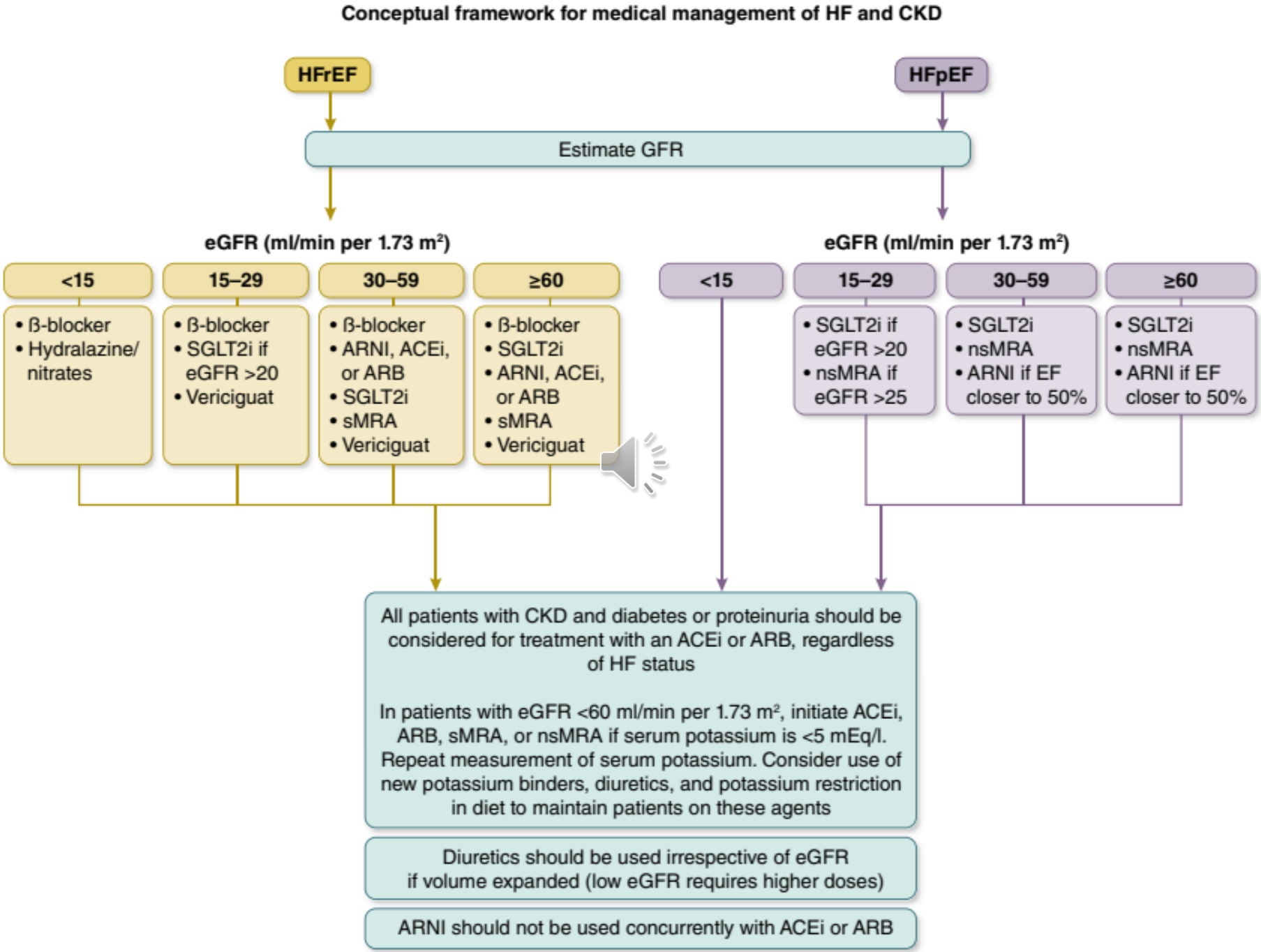
Carolyn S.P. Lam[1], Biykem Bozkurt[2,3], David Z.I. Cherney[4], Justin A. Ezekowitz[5], Meg J. Jardine[6,7], Sadiya S. Khan[8,9], Magdalena Madero[10], Mark J. Sarnak[11], Jozine M. ter Maaten[12], Michael Cheung[13], Jennifer M. King[13], Morgan E. Grams[14], Michel Jadoul[15] and Nisha Bansal[16]; for Conference Participants[17]

JACC Heart Fail. 2026 April ; 14(4): 102943. doi:10.1016/j.jchf.2026.102943.

Kidney Disease and Heart Failure: Recent Advances and Current Challenges:

Conclusions From a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference

Carolyn S.P. Lam[a], Biykem Bozkurt[b,c], David Z.I. Cherney[d], Justin A. Ezekowitz[e], Meg J. Jardine[f,g], Sadiya S. Khan[h,i], Magdalena Madero[j], Mark J. Sarnak[k], Jozine M. ter Maaten[l], Michael Cheung[m], Jennifer M. King[m], Morgan E. Grams[n], Michel Jadoul[o], Nisha Bansal[p] for Conference Participants

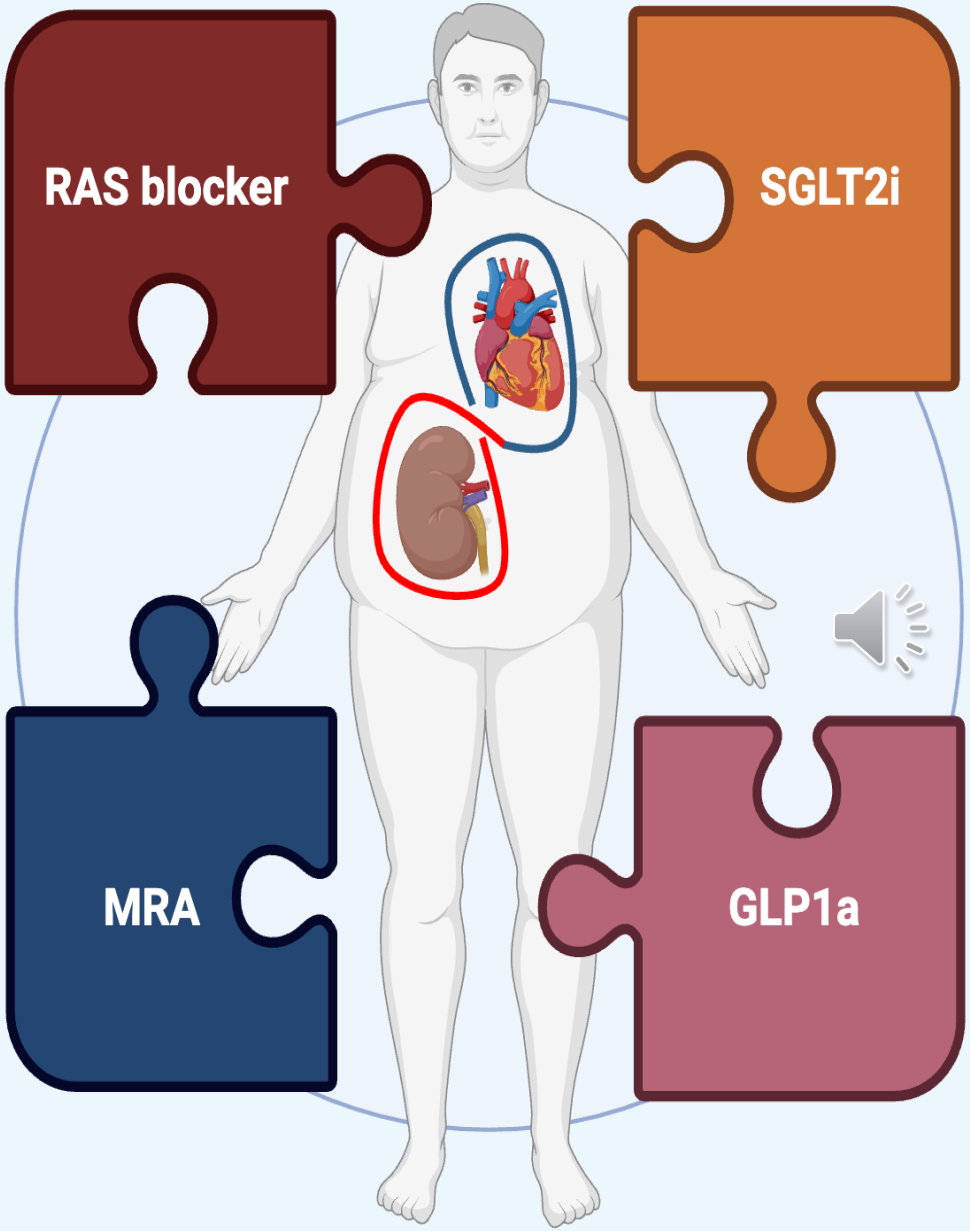

Conceptual framework for medical management of HF and CKD
HFrEF
HFpEF
Estimate GFR
eGFR (ml/min per 1.73 m²)
<15
15–29
30–59
≥60
• ß-blocker
• Hydralazine/ nitrates
• ß-blocker
• SGLT2i if eGFR >20
• Vericiguat
• ß-blocker
• ARNI, ACEi, or ARB
• SGLT2i
• sMRA
• Vericiguat
• ß-blocker
• SGLT2i
• ARNI, ACEi, or ARB
• sMRA
• Vericiguat
eGFR (ml/min per 1.73 m²)
<15
15–29
30–59
≥60
• SGLT2i if eGFR >20
• nsMRA if eGFR >25
• SGLT2i
• nsMRA
• ARNI if EF closer to 50%
• SGLT2i
• nsMRA
• ARNI if EF closer to 50%
All patients with CKD and diabetes or proteinuria should be considered for treatment with an ACEi or ARB, regardless of HF status
In patients with eGFR <60 ml/min per 1.73 m², initiate ACEi, ARB, sMRA, or nsMRA if serum potassium is <5 mEq/l. Repeat measurement of serum potassium. Consider use of new potassium binders, diuretics, and potassium restriction in diet to maintain patients on these agents
Diuretics should be used irrespective of eGFR if volume expanded (low eGFR requires higher doses)
ARNI should not be used concurrently with ACEi or ARB

GDMT for Everyone

Abbreviations | Legend

Class I pillars of HFrEF GDMT across the span of kidney disease

Class	Medication	ESKD	CKD 5	CKD 4	CKD 3B	CKD 3A	CKD 1-2	AKI
ACEI	**Lisinopril**	Renally-dose	Renally-dose	OK	OK	OK	OK	Contraindicated
ARB	**Losartan**	OK	OK	OK	OK	OK	OK	Contraindicated
ARNI	**Sacubitril-valsartan**	Not enough data	Renally-dose	Renally-dose	OK	OK	OK	Contraindicated
BBs	**Metoprolol**	OK	OK	OK	OK	OK	OK	OK
	Carvedilol	OK	OK	OK	OK	OK	OK	OK
	Bisoprolol	OK	Renally-dose	Renally-dose	Renally-dose	OK	OK	OK
Loop diuretics	**Furosemide**	Case-Dependent	OK	OK	OK	OK	OK	Case-Dependent
	Torsemide	Case-Dependent	OK	OK	OK	OK	OK	Case-Dependent
	Bumetanide	Case-Dependent	OK	OK	OK	OK	OK	Case-Dependent
MRA	**Spironolactone**	Contraindicated	Contraindicated	Contraindicated	Renally dose	OK	OK	Contraindicated
	Eplerenone	Contraindicated	Contraindicated	Contraindicated	Renally dose	OK	OK	Contraindicated
	Finerenone	Contraindicated	Contraindicated	Contraindicated	Renally dose	Renally dose	OK	Contraindicated
SGLT2i	**Dapagliflozin**	Contraindicated	Caution	Caution	OK	OK	OK	Caution
	Empagliflozin	Contraindicated	Caution	Caution	OK	OK	OK	Caution
Nitrate	Isosorbide mononitrate	OK	OK	OK	OK	OK	OK	OK
	Isosorbide dinitrate	OK	OK	OK	OK	OK	OK	OK
Vasodilator	Hydralazine	OK	OK	OK	OK	OK	OK	OK
Class	**Medication**	**ESKD**	**CKD 5**	**CKD 4**	**CKD 3B**	**CKD 3A**	**CKD 1-2**	**AKI**



Pillar Therapy In Cardiorenal Syndrome

(ACEI or ARBs) or ARNIs	Beta-blockers	SGLT2Inh	MRAs (s. or ns)	GLP1 RA

Diuretics

Thresholds for initiating guideline-directed medical therapy in HF and kidney disease

Therapy	Eligibility based on kidney function		Management of adverse effects
	CKD guidance[a]	HF guidance[b]	
SGLT2I	eGFR > 20 ml/min per 1.73 m^2 in those with CKD and DM eGFR > 20 ml/min per 1.73 m^2 in those with CKD and UACR > 200 mg/g (20 mg/mmol) eGFR 20–45 ml/min per 1.73 m^2 in those with CKD and UACR <200 mg/g (20 mg/mmol)	eGFR > 20 ml/min per 1.73 m^2	Hyperkalemia with RAASi, steroidal and nsMRA, and ARNI may be mitigated by • Concomitant SGLT2i • Potassium binders • Correction of acidosis • Moderation of dietary potassium intake • Review and adjustment of concurrent medications • Diuretics
nsMRA (finerenone)	Type 2 diabetes, eGFR > 25 ml/min per 1.73 m^2, and UACR > 30 mg/g despite standard care	(As for the treatment of comorbid diabetic CKD)	eGFR "dip" with SGLT2i, RAASi, steroidal and nsMRA, and ARNI: • Hemodynamic fluctuations in eGFR up to 30% can be seen and should not lead to discontinuation • If >30%, other causes of AKI should be evaluated
GLP-1 RA	Type 2 diabetes, eGFR ≥ 25 ml/min per 1.73 m^2, and elevated UACR despite standard care Initiation for glycemia lowering down to 15 ml/min per 1.73 m^2	(As for the treatment of comorbid type 2 diabetes)	
ARNI	If eGFR <30 ml/min per 1.73 m^2, reduced dose should be started and titrated up	eGFR > 30 ml/min per 1.73 m^2	
ACEi or ARB	All persons with CKD, and moderate or severe albuminuria in persons with and without diabetes Should be continued in CKD even when eGFR declines to <30 ml/min per 1.73 m^2	Serum creatinine <221 µmol/l (<2.5 mg/dl) or eGFR > 30 ml/min per 1.73 m^2	
Steroidal MRA	May be used for the treatment of HF in CKD but have a higher risk of adverse effects (nsMRA preferred)	Serum creatinine <221 µmol/l (<2.5 mg/dl) or eGFR > 30 ml/min per 1.73 m^2	

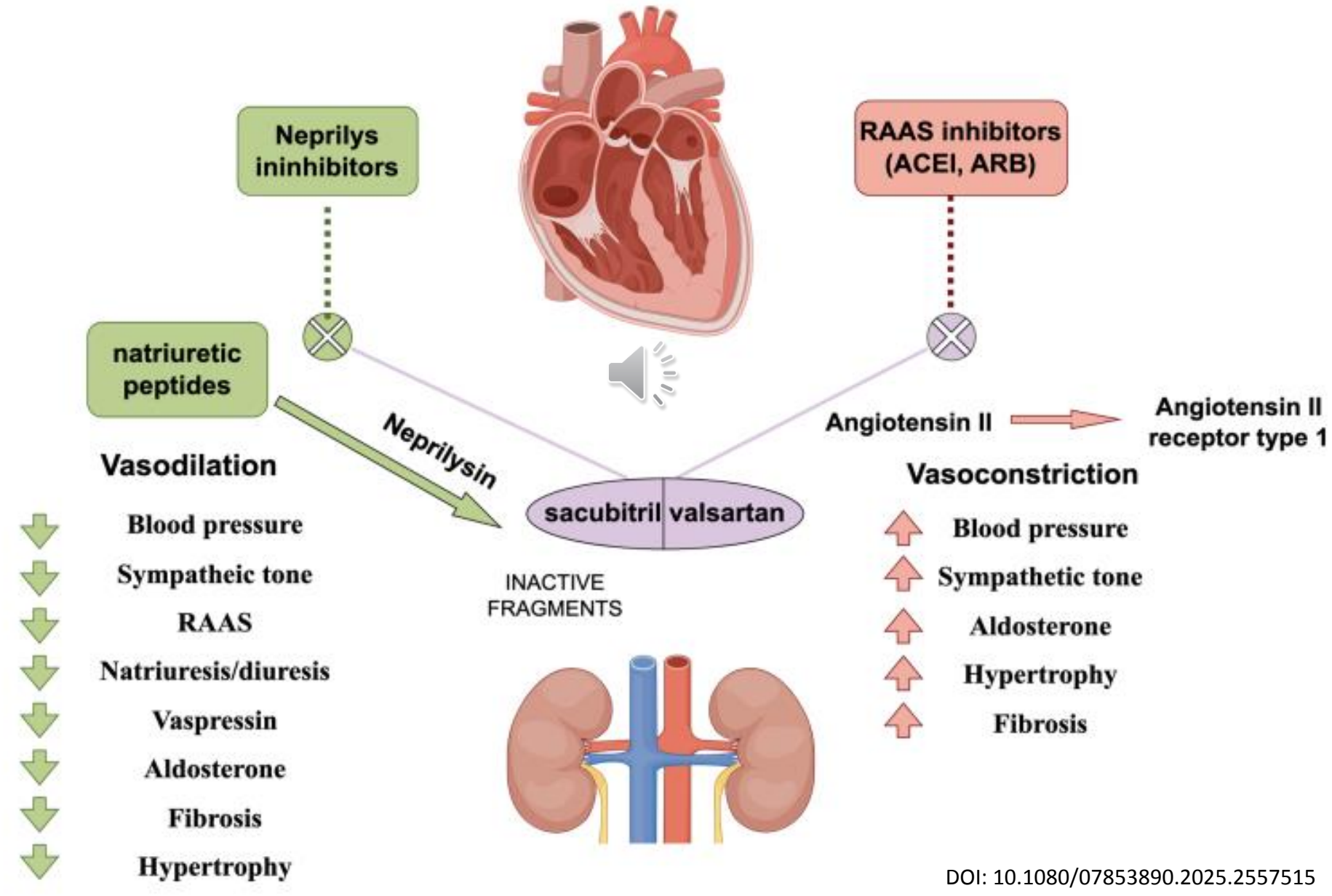
https://doi.org/10.1016/ j.kint.2025.10.011

Advancing Cardiorenal Interaction: From Pathophysiological Paradigms to Novel Therapeutic Strategies

Kidney Dis. 2025;11(1):695-711. doi:10.1159/000548367

Cardiorenal Medicine	RAASi	ARNI	SGLT2i	ns-MRA	GLP-1 RA
					
Renal hemodynamics	Vasodilation E>A eGFR↓ Albuminuria↓	Vasodilation E=A eGFR no change Albuminuria↑	Vasoconstriction A eGFR↓ Albuminuria↓	Vasodilation E>A eGFR↓ Albuminuria↓	Vasoconstriction A eGFR↓ Albuminuria↓
Side effects	Hyperkelamia	Hyperkelamia	Genital infections	Hyperkelamia	GI reaction
BP/BG effect	BP reduction	BP reduction	BG reduction	BP reduction	BG reduction
Cardiac outcomes	MACE↓ (CV death, nonfatal stroke,MI, HFH)	NT-proBNP↓ CV death↓ HFH↓	MACE↓	MACE↓	HFH↓
Renal outcomes	Slow the rate of eGFR decline, proteinuria, and renal cause of death	Slow the rate of eGFR decline, with the risk of increase in UACR	Slow the rate of eGFR decline, proteinuria, and renal cause of death	Slow the rate of eGFR decline, and proteinuria	Decrease renal composite outcomes (incident macro-albuminuria, sustained decrease in eGFR, RRT, renal cause of death)

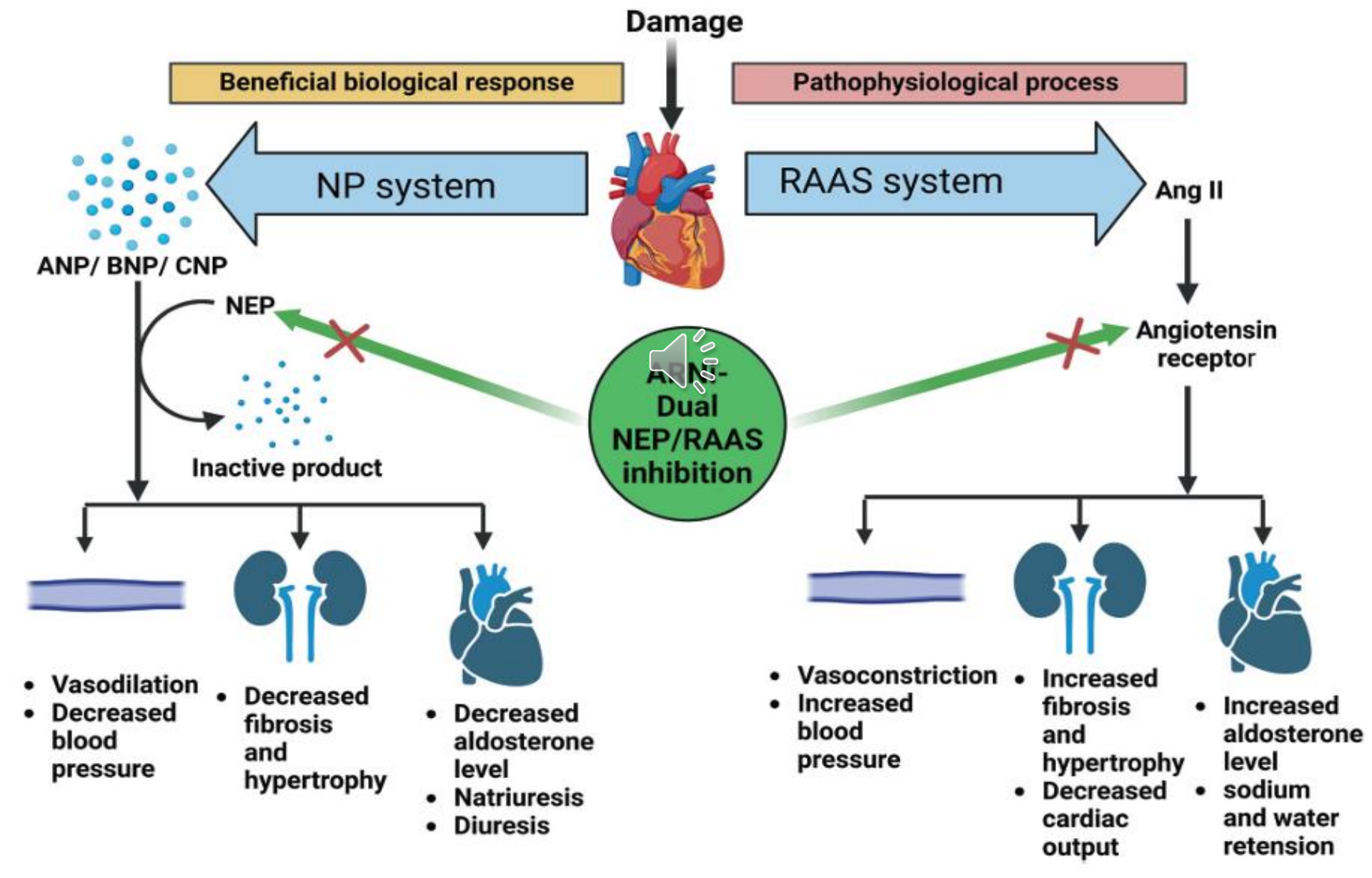
Pharmacological mechanisms of sacubitril/valsartan



DOI: 10.1080/07853890.2025.2557515

Schematic representation of the mechanism of action of ARNi

https://doi.org/10.1038/s41440-024-01989-w



PARAGON-HF TRIAL

Solomon SS et al. Angiotensin–Neprilysin Inhibition in Heart Failure with Preserved Ejection Fraction. N Engl J Med. 2019;381(17):1609-1620. doi:10.1056/nejmoa1908655

Sacubitril
Neprilysin-inhibitor
↑ Vasodilation + ↑ Diuresis

Valsartan
Angiotensin Receptor Blocker
↓ Vasoconstriction + ↓ Na retention

Inclusion Criteria
Age ≥ 50
EF ≥ 45 %
NYHA II-IV
Structural Heart Disease
Diuretic therapy
↑ Natriuretic Peptides

Question
In patients with HFpEF (EF ≥ 45%), will sacubitril-valsartan (ARNI) result in ↓ CV mortality and HF hospitalizations compared to valsartan (ARB) alone?

N = 4,822

ARNI N = 2,407
OR
ARB N = 2,389

1° Outcome	2° Outcome	2° Outcome
HF hospitalization + CV mortality	All-Cause Mortality	ESRD, Renal Failure, Worsening GFR
RR 0.87; P = 0.06 95% CI: 0.75-1.01	HR 0.97 95% CI: 0.84 to 1.13	HR 0.5 95% CI: 0.33 to 0.77
ARNI 37% (894) ARB 42.4% (1009)	ARNI 14.2% (342) ARB 14.6% (349)	ARNI 1.4% (33) ARB 2.7% (64)

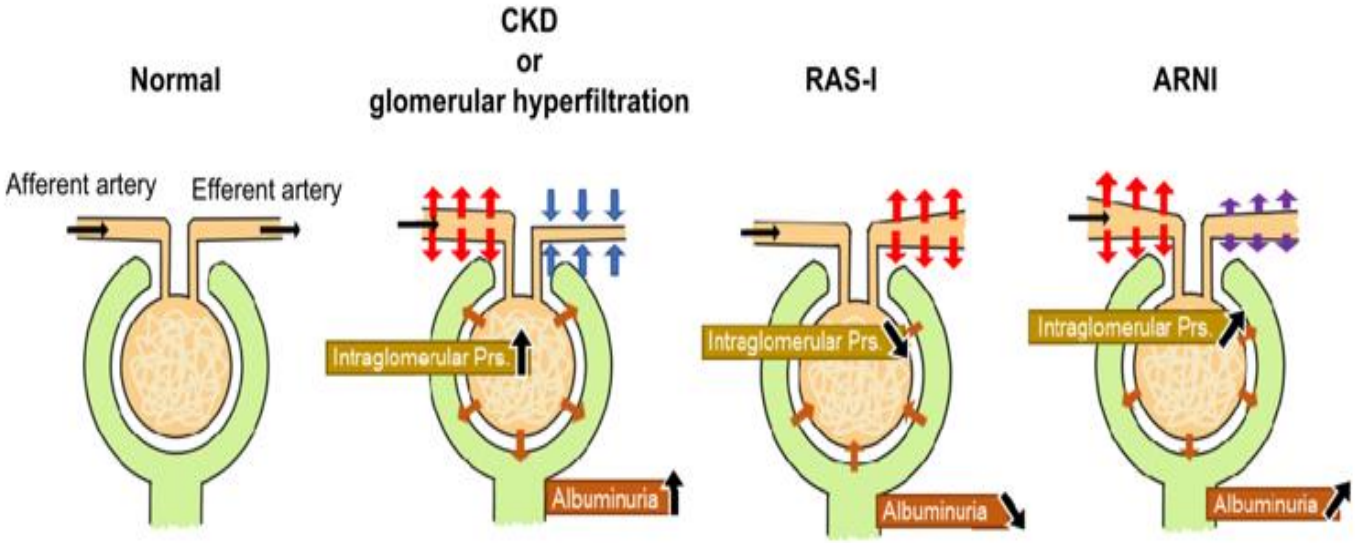
Conclusions
In patients with HFpEF, ARNI was not associated with ↓ CV mortality and HF hospitalizations.

@najahakhan | Edited by: @evelynsongmd

PARADIGM HF Trial

Prospective Comparison of **ARNI** [Angiotensin Receptor - Neprilysin Inhibitor] with **ACEI** [Angiotensin Converting Enzyme Inhibitor] to **D**etermine **I**mpact on **G**lobal **M**ortality and Morbidity in **H**eart **F**ailure Trial.

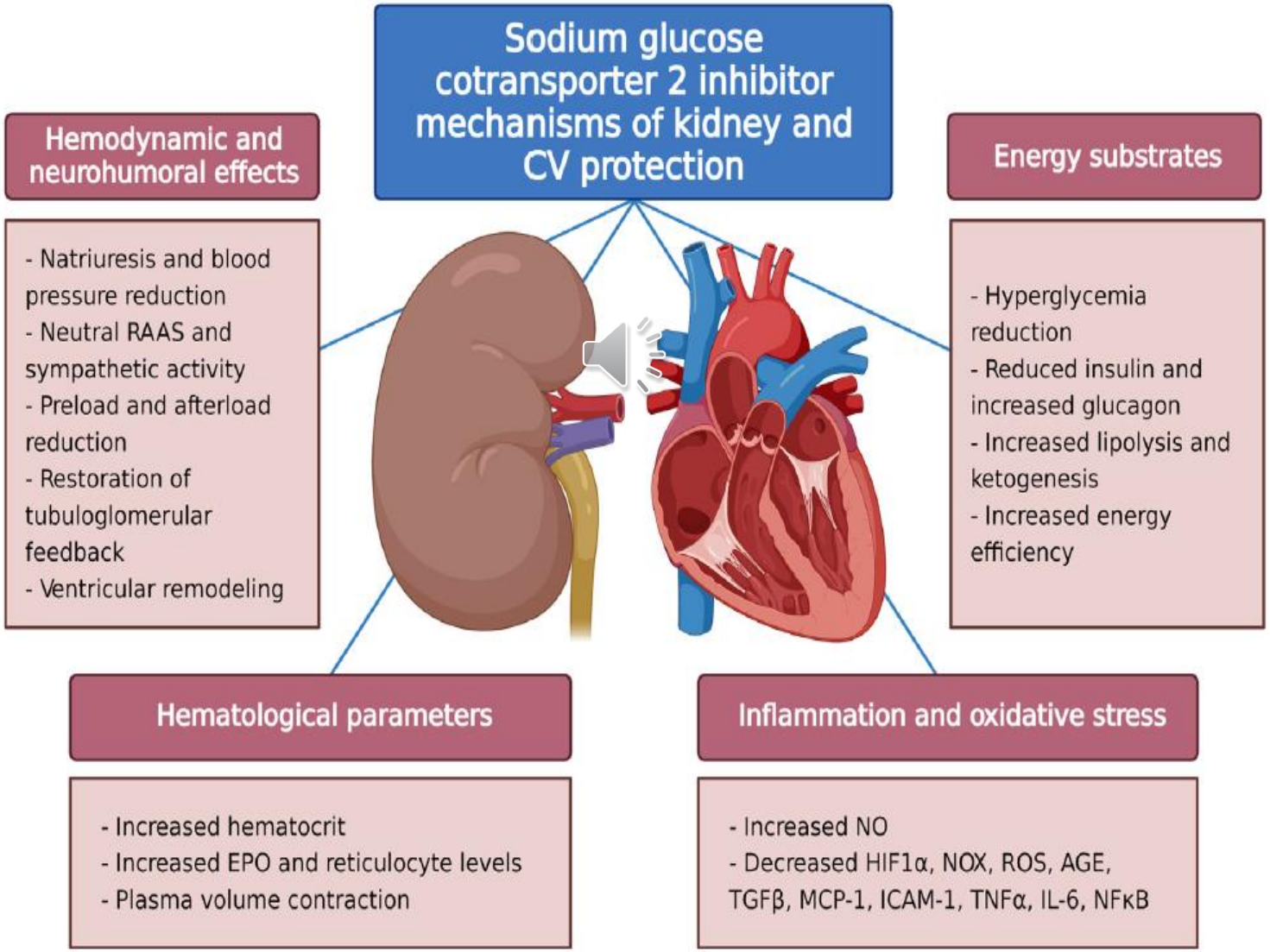
ANGIOTENSIN Receptor –**NEPRILYSIN** Inhibition
versus
ENALAPRIL in Heart Failure



Shunichiro Tsukamoto. Journal of the American Heart Association. Updates for Cardio-Kidney Protective Effects by Angiotensin Receptor-Neprilysin Inhibitor: Requirement for Additional Evidence of Kidney Protection, Volume: 12, Issue: 8, DOI: (10.1161/JAHA.122.029565)

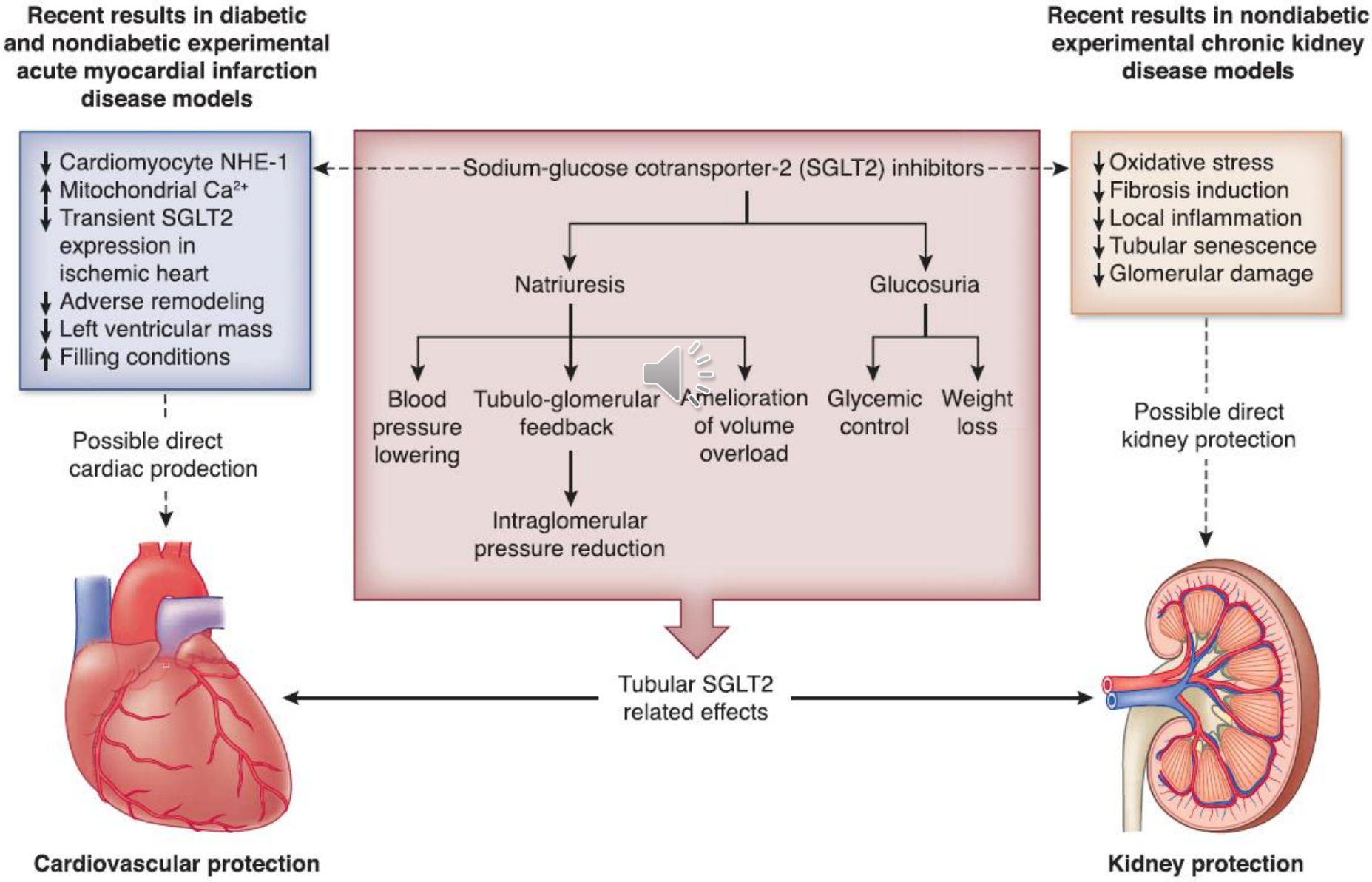
Potential mechanism behind the cardiovascular and kidney protective effects of SGLT2 inhibitors.

https://doi.org/10.1016/j.metabol.2021.154918



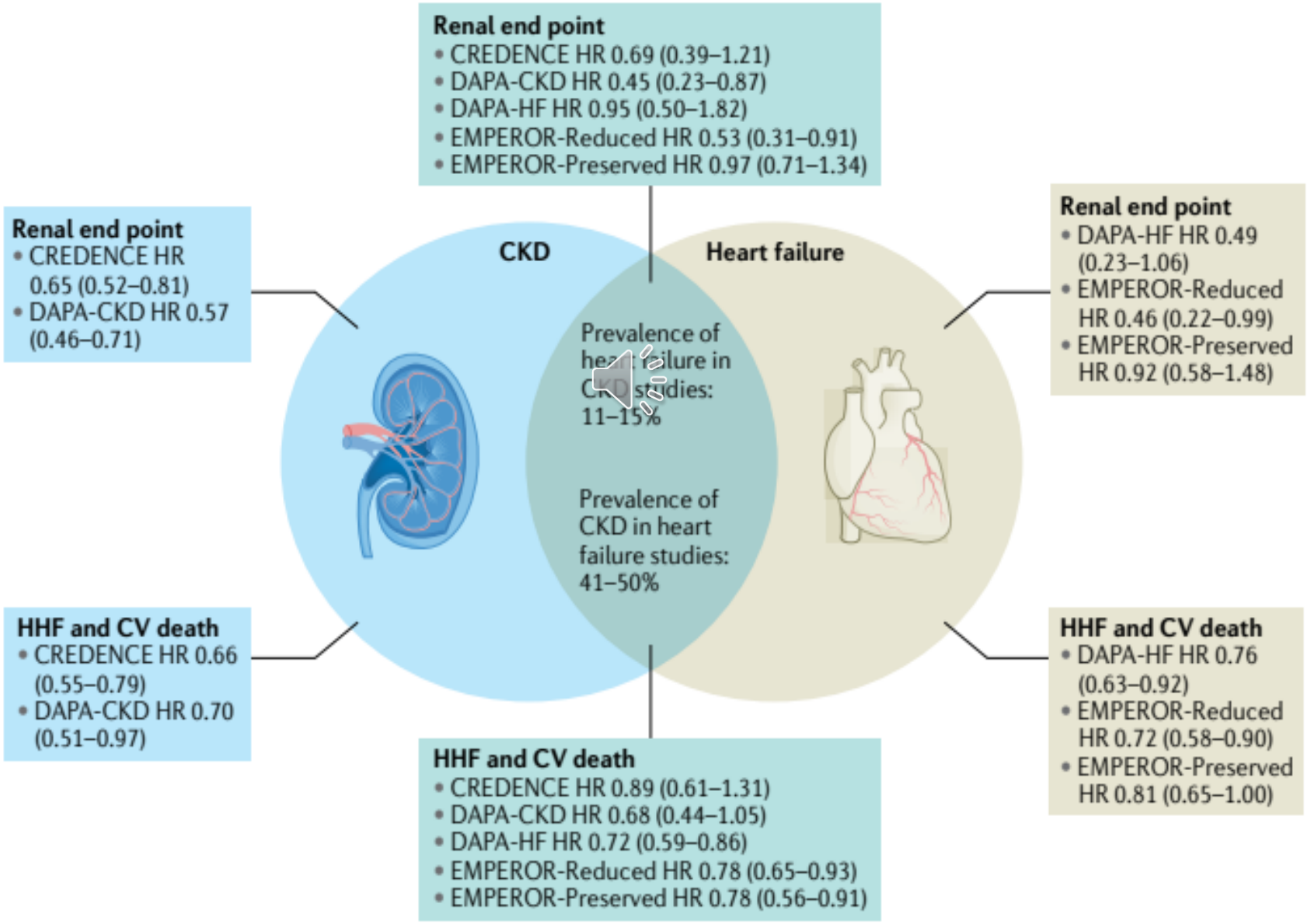
Potential cardiorenal protective mechanisms for SGLT inhibition mediated via tubular SGLT2 and via mechanisms working direct on the heart and the kidney

https://doi.org/10.2215/CJN.0000000000000221



SGLT2 Inhibitors and Clinical Trials

https://doi.org/10.1038/s41581-022-00535-6



FINERENONE (KERENDIA®): FROM DEVELOPMENT TO GUIDELINE-INTEGRATED CARE

A Non-steroidal MRA for the Cardio-Renal Continuum

EARLY DEVELOPMENT

Proof of concept, dose-finding, safety and PK

2010–2014

Early Clinical Studies

ARTS
ARTS-DN
ARTS-HF
ARTS-HF Japan

Established safety, pharmacology and early signals of cardio-renal benefit

PIVOTAL CKD OUTCOME TRIALS

T2DM and CKD populations

2015–2021

Key Trials

FIDELIO-DKD
FIGARO-DKD

Integrated Evidence

FIDELITY
(pooled analysis)

Demonstrated reduction in kidney disease progression and major cardiovascular outcomes

REGULATORY APPROVAL

2021

FDA Approval
July 9, 2021

Indication:
Chronic kidney disease associated with type 2 diabetes

To reduce risk of kidney disease progression and cardiovascular events

GUIDELINE INTEGRATION

2022

ADA Standards of Care 2022

KDIGO 2022 Diabetes in CKD Guideline

Recommended for patients with T2DM and CKD (albuminuria) on maximized ACEi/ARB with persistent risk

HEART FAILURE EXPANSION

2023–2024+

HF Outcome Evidence

FINEARTS-HF

Exploring broader HF spectrum (HFpEF / HFmrEF) and cardiorenal benefit

Supporting incorporation into heart failure guidelines and expanding clinical role

REGULATORY MILESTONES

- **Jul 9, 2021** — FDA Approval (United States)
- **Feb 2022** — EMA Approval (Europe)
- **2023–2024+** — Ongoing global expansion

GUIDELINE MILESTONES

- **2022** — ADA Standards of Care
- **2022** — KDIGO Diabetes in CKD Guideline
- **2023** — ESC Heart Failure Guideline Update
- **2024+** — Further updates anticipated

KEY TAKE-HOME MESSAGE

Finerenone has evolved from early clinical exploration to a proven cardiorenal therapy. Supported by ARTS studies, FIDELIO-DKD, FIGARO-DKD and FIDELITY, approved in 2021, and integrated into ADA and KDIGO guidelines in 2022, with expanding evidence in heart failure through FINEARTS-HF.

POSITIONING TODAY

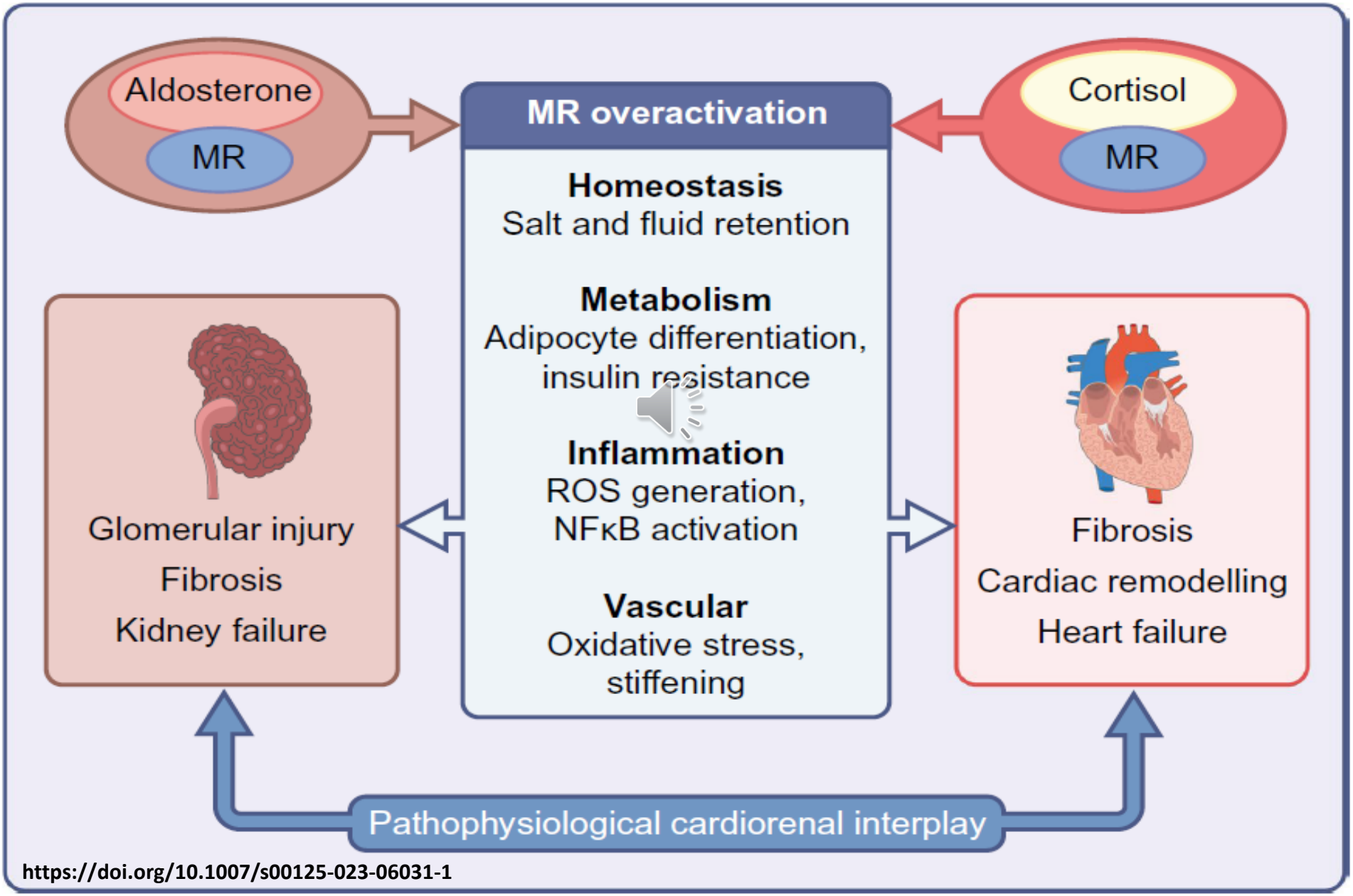
A key non-steroidal MRA for patients across the cardio-renal spectrum

PK = pharmacokinetics; MRA = mineralocorticoid receptor antagonist; T2DM = type 2 diabetes mellitus; CKD = chronic kidney disease;
ACEi = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; HFpEF = heart failure with preserved ejection fraction; HFmrEF = heart failure with mildly reduced ejection fraction.

In patients already receiving optimized cardiorenal GDMT, to what extent does targeting mineralocorticoid receptor–mediated inflammation and fibrosis with finerenone further reduce residual cardiorenal risk? And ultimately, does this translate into merely incremental benefit…

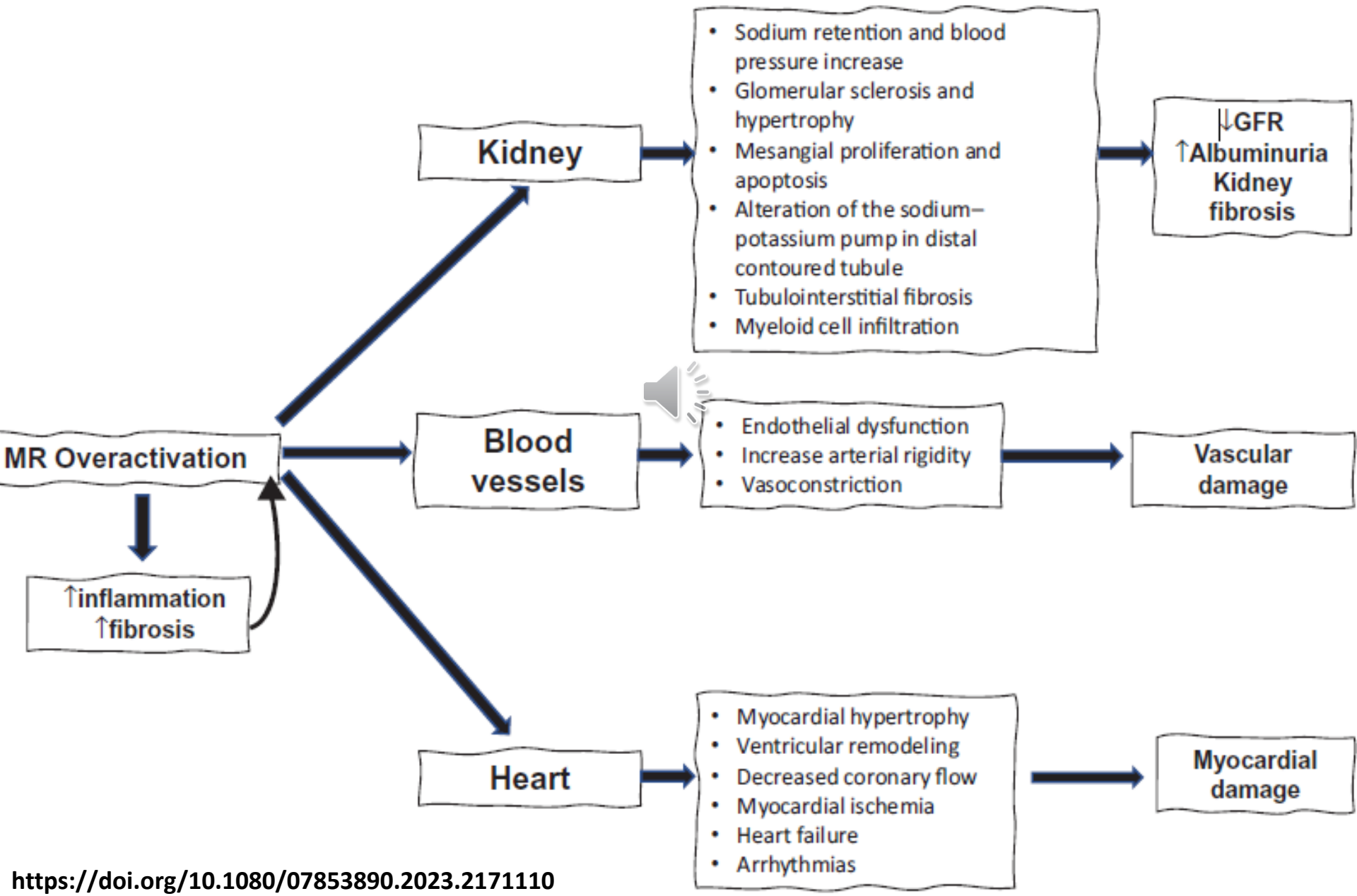
Does finerenone truly represent a game changer in cardiorenal medicine?

Role of MR overactivation in cardiorenal disease



https://doi.org/10.1007/s00125-023-06031-1

Role of MR overactivation in cardiorenal disease

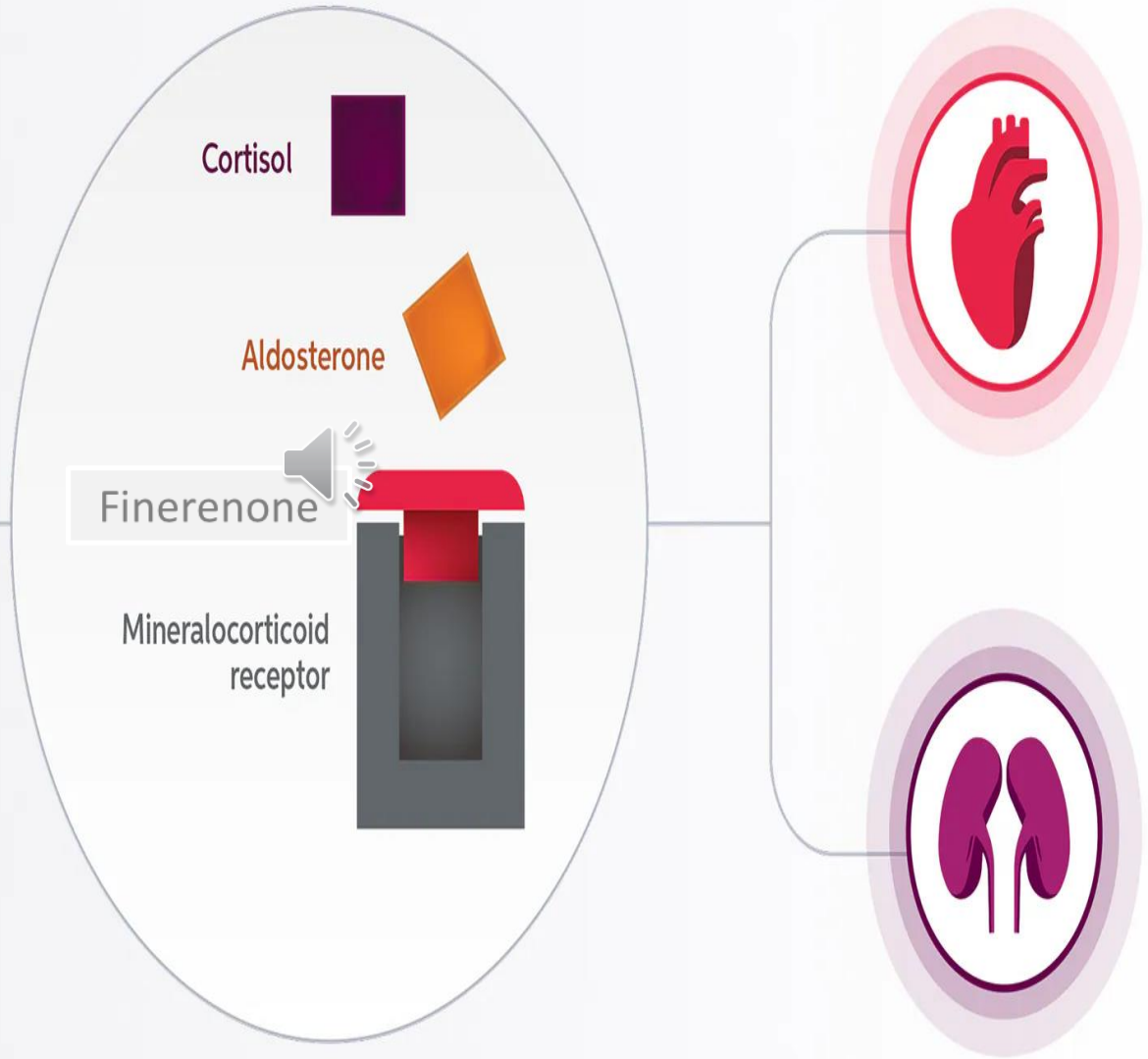


https://doi.org/10.1080/07853890.2023.2171110

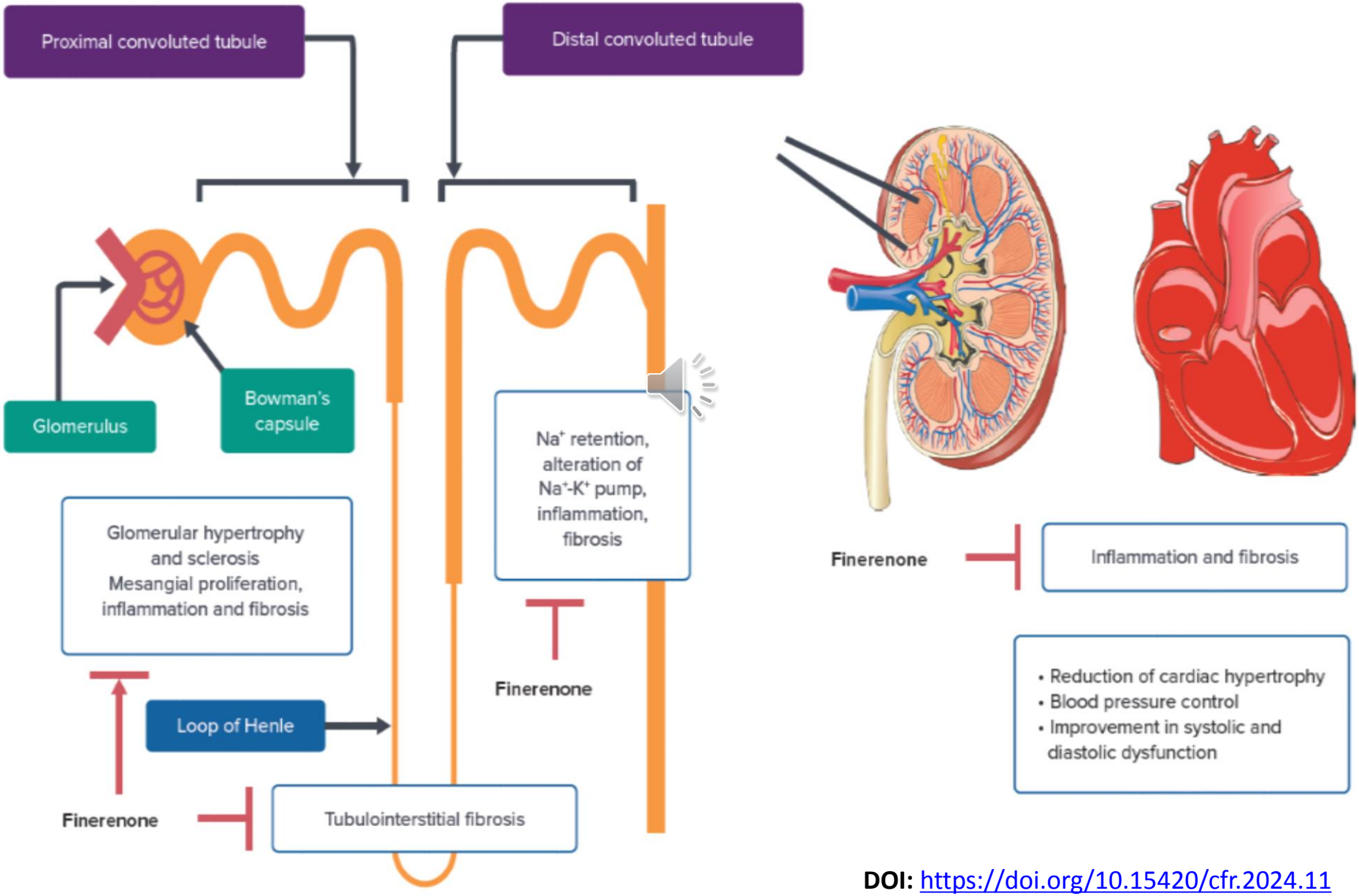
Overactivation of the MR is thought to contribute to[1,5,6]:

- Sodium & fluid retention
- Inflammation
- Fibrosis
- Cardiac hypertrophy

Finerenone selectively blocks the MR in both the heart and kidneys[1,5,6]

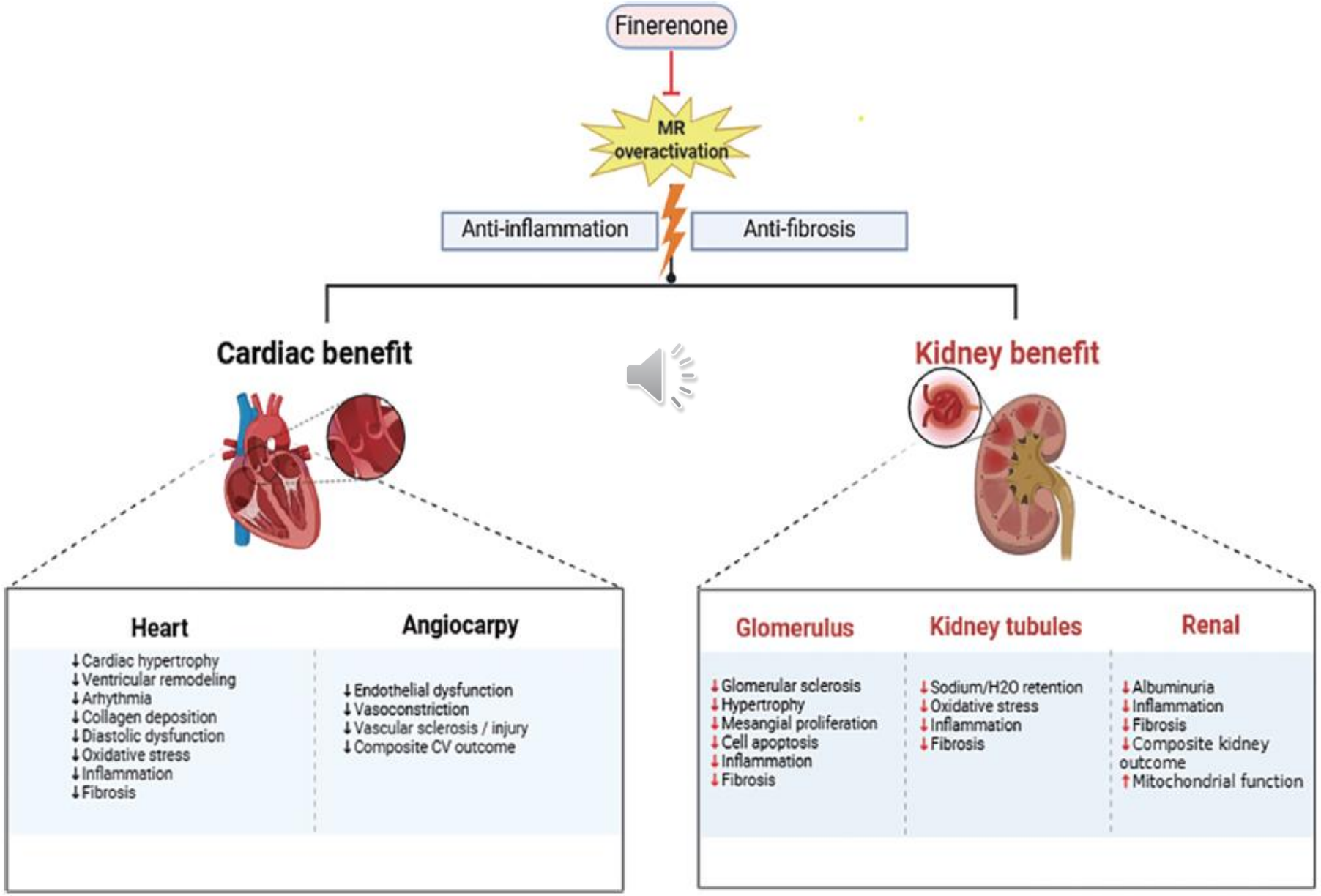


Mechanism of Action of Finerenone on the Heart and Kidneys



DOI: https://doi.org/10.15420/cfr.2024.11

Finerenone targets mineralocorticoid receptor: Dual cardiac and renal benefits



https://doi.org/10.53941/ijddp.2025.100019

Characteristics of Mineralocorticoid Receptor Antagonists

https://doi.org/10.53941/ijddp.2025.100019

Characteristics	Spironolactone	Eplerenone	Finerenone	Embodiment of Advantages
Structural properties	Flat (Steroidal)	Flat (Steroidal)	Bulky (Non-steroidal)	Kidney and heart dual benefits, Stronger anti-inflammatory and anti-fibrotic effects
Tissue distribution	Kidney >> Heart	Kidney > Heart	Kidney = Heart	
MR affinity	High (+++)	Low (+)	High (+++)	
Half-life (hours)	Long (>20)	Medium (3–6)	Short (2–4)	
Absorption	100% bioavailable	69% bioavailable	44% bioavailable	Lower risk of hyperkalemia
Metabolites	Active metabolites	No active	No active	
MR selectivity	Low (+)	Medium (++)	High (+++)	
Adverse reaction	Hyperkalemia, Hypolibido, Gynecomastia, Sexual dysfunction	Hyperkalemia, Hyponatremia, Hyperlipidemia	Hyperkalemia, No other major adverse reactions were observed	Lower risk of hormone-related adverse reactions

Recommendation 3.8.1: We suggest a nonsteroidal mineralocorticoid receptor antagonist with proven kidney or cardiovascular benefit for adults with T2D, an eGFR >25 ml/min per 1.73 m^2, normal serum potassium concentration, and albuminuria (>30 mg/g [>3 mg/mmol]) despite maximum tolerated dose of RAS inhibitor (RASi) *(2A)*.

Practice Point 3.8.1: Nonsteroidal MRA are most appropriate for adults with T2D who are at high risk of CKD progression and cardiovascular events, as demonstrated by persistent albuminuria despite other standard-of-care therapies.

Practice Point 3.8.2: A nonsteroidal MRA may be added to a RASi and an SGLT2i for treatment of T2D and CKD in adults.

Practice Point 3.8.3: To mitigate risk of hyperkalemia, select people with consistently normal serum potassium concentration and monitor serum potassium regularly after initiation of a nonsteroidal MRA (Figure 26).

Practice Point 3.8.4: The choice of a nonsteroidal MRA should prioritize agents with documented kidney or cardiovascular benefits.

Practice Point 3.8.5: A steroidal MRA may be used for treatment of heart failure, hyperaldosteronism, or refractory hypertension, but may cause hyperkalemia or a reversible decline in glomerular filtration, particularly among people with a low GFR.

KDIGO 2024 CLINICAL PRACTICE GUIDELINE FOR THE EVALUATION AND MANAGEMENT OF CHRONIC KIDNEY DISEASE

1 Getting started

Measure serum K+ and eGFR before dose initiation
DO NOT INITIATE if serum K+ is >5.0 mEq/L* or if eGFR is <25 mL/min/1.73 m²

CKD Associated with T2D

	eGFR (mL/min/1.73 m²)	
	≥25 to <60	≥60
Starting dose	 10 mg	 20 mg
Target daily dose	 20 mg	 20 mg

The recommended starting dose and target daily dose is based on initial eGFR and serum K+ thresholds.

Not actual size.

2 Dose modifications

Measure serum K+ and eGFR levels 4 weeks after initiation, restart, or dose adjustment
WITHHOLD TREATMENT if serum K+ is >5.5 mEq/L and consider restarting at 10 mg once serum K+ is ≤5.0 mEq/L

Serum K+ level	Dose adjustment
≤4.8 mEq/L	Increase to† or maintain at target dose
>4.8 to 5.5 mEq/L	Maintain current dose

1 Getting started

Measure serum K+ and eGFR before dose initiation
DO NOT INITIATE if serum K+ is >5.0 mEq/L or if eGFR is <25 mL/min/1.73 m²

HF EF≥40%	eGFR (mL/min/1.73 m²)	
	≥25 to <60	≥60
Starting dose	 10 mg	 20 mg
Target daily dose	 20 mg	 40 mg

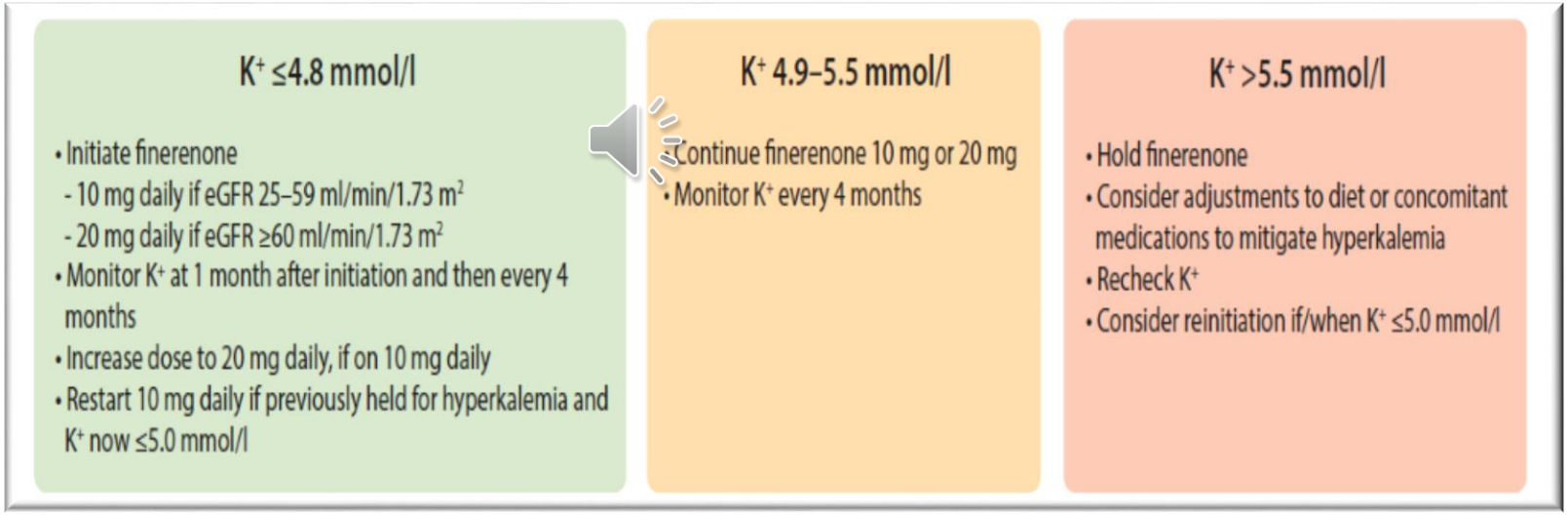
The recommended starting dose and target daily dose is based on initial eGFR and serum K+ thresholds. Not actual size.

2 Dose modifications

Measure serum K+ and eGFR levels 4 weeks after initiation, restart, or dose adjustments
WITHHOLD TREATMENT if serum K+ is ≥6.0 mEq/L and restart at 10 mg once serum K+ is <5.5 mEq/L*

Serum K+ level	Dose adjustment
<5.0 mEq/L	Increase to† or maintain at target dose
≥5.0 to <5.5 mEq/L	Maintain current dose
≥5.5 to <6.0 mEq/L	Decrease dose to previous strength‡

Serum potassium monitoring during treatment with a nonsteroidal mineralocorticoid receptor antagonist (MRA) (finerenone)

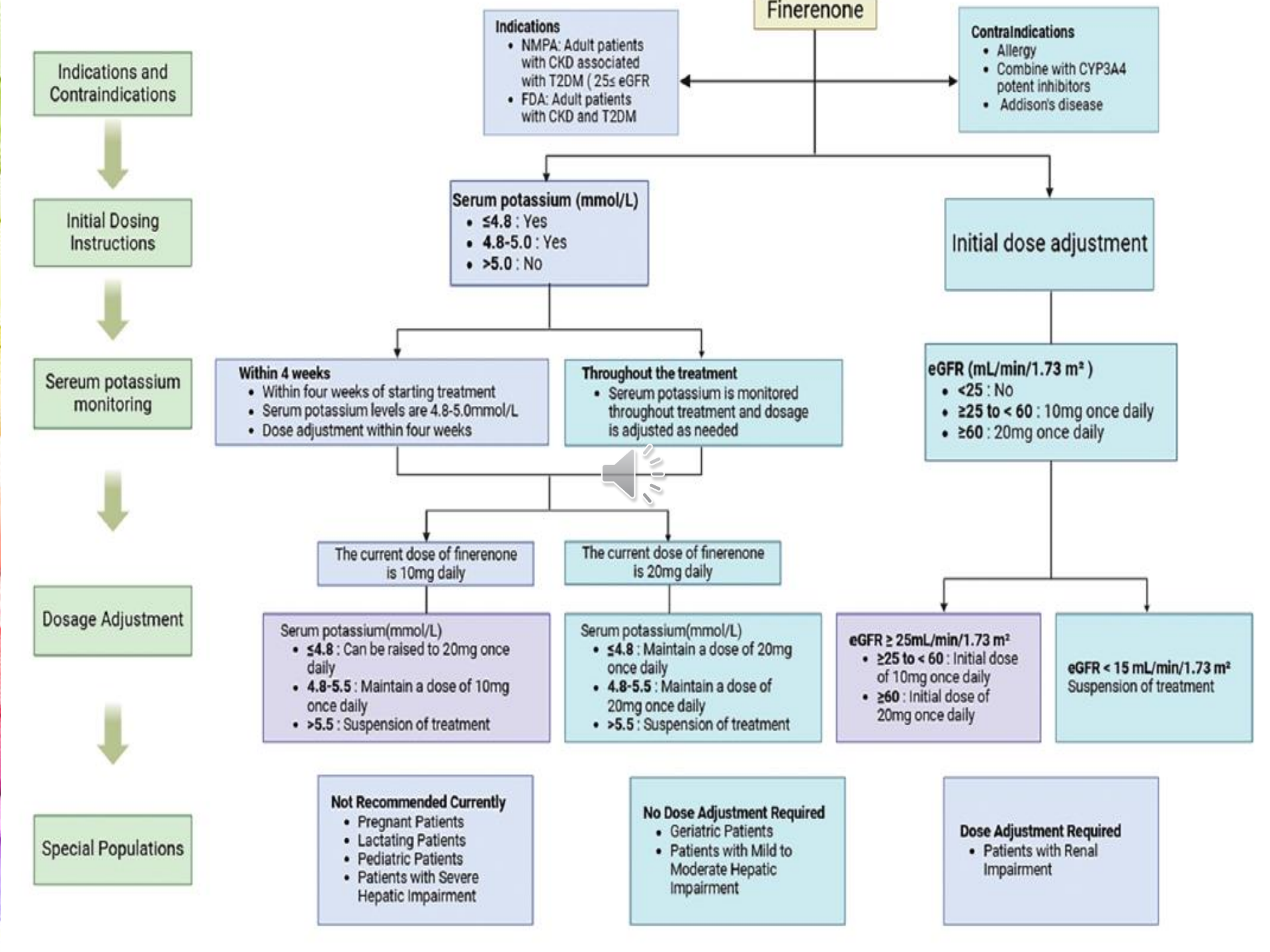


KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease

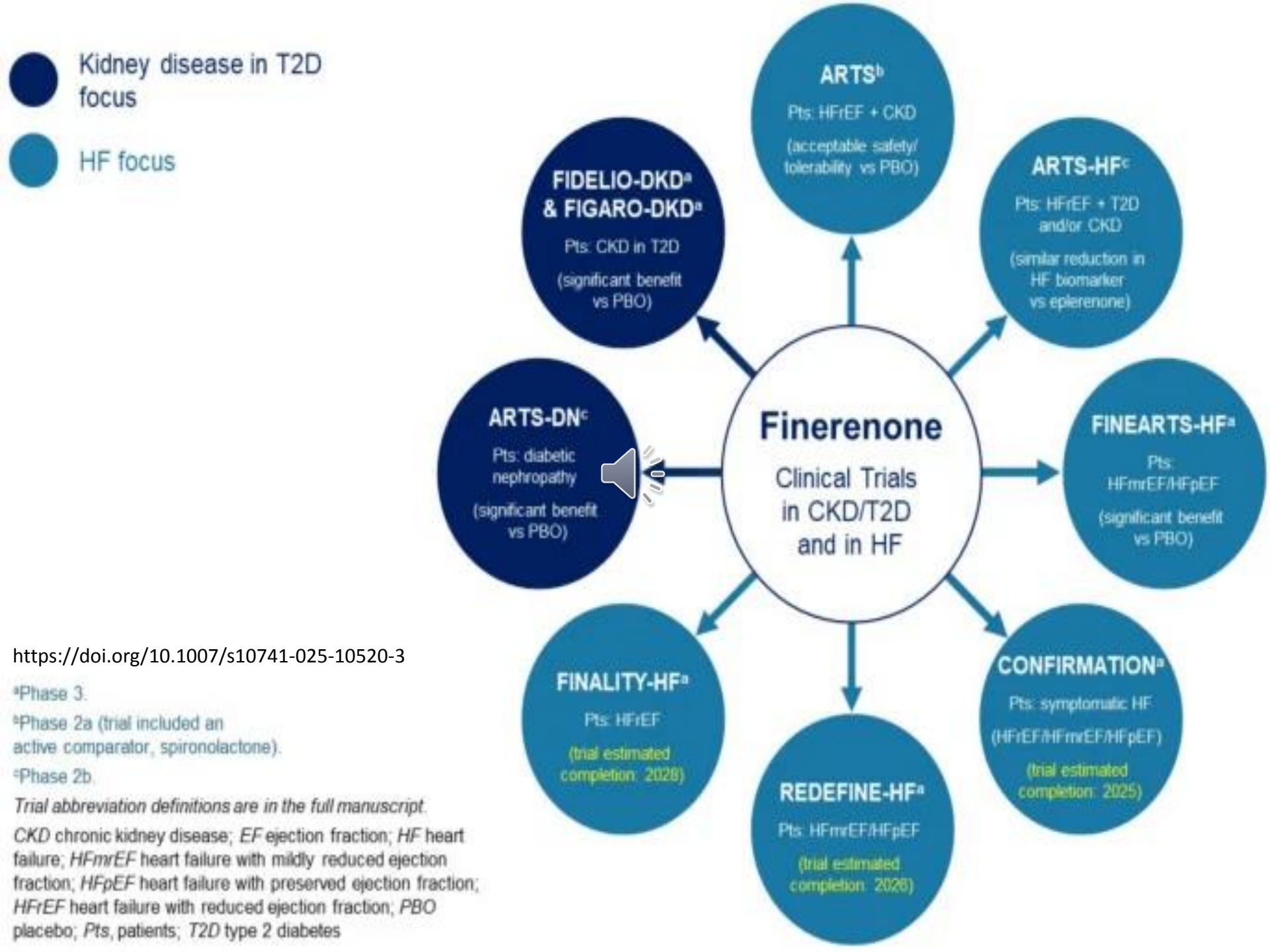
Drug Interactions with Finerenone

Finerenone is primarily metabolized by: CYP3A4
Therefore, the most important interactions involve:

- **CYP3A4 Inhibitors**
- **CYP3A4 Inducers**
- **potassium-elevating drugs**
- **Dual RAAS blockade**


Finerenone
Indications and Contraindications
Initial Dosing Instructions
Sereum potassium monitoring
Dosage Adjustment
Special Populations
Indications
NMPA: Adult patients with CKD associated with T2DM (25≤ eGFR
FDA: Adult patients with CKD and T2DM
ContraIndications
Allergy
Combine with CYP3A4 potent inhibitors
Addison's disease
Serum potassium (mmol/L)
≤4.8 : Yes
4.8-5.0 : Yes
>5.0 : No
Initial dose adjustment
Within 4 weeks
Within four weeks of starting treatment
Serum potassium levels are 4.8-5.0mmol/L
Dose adjustment within four weeks
Throughout the treatment
Sereum potassium is monitored throughout treatment and dosage is adjusted as needed
eGFR (mL/min/1.73 m²)
<25 : No
≥25 to < 60 : 10mg once daily
≥60 : 20mg once daily
The current dose of finerenone is 10mg daily
The current dose of finerenone is 20mg daily
Serum potassium(mmol/L)
≤4.8 : Can be raised to 20mg once daily
4.8-5.5 : Maintain a dose of 10mg once daily
>5.5 : Suspension of treatment
Serum potassium(mmol/L)
≤4.8 : Maintain a dose of 20mg once daily
4.8-5.5 : Maintain a dose of 20mg once daily
>5.5 : Suspension of treatment
eGFR ≥ 25mL/min/1.73 m²
≥25 to < 60 : Initial dose of 10mg once daily
≥60 : Initial dose of 20mg once daily
eGFR < 15 mL/min/1.73 m²
Suspension of treatment
Not Recommended Currently
Pregnant Patients
Lactating Patients
Pediatric Patients
Patients with Severe Hepatic Impairment
No Dose Adjustment Required
Geriatric Patients
Patients with Mild to Moderate Hepatic Impairment
Dose Adjustment Required
Patients with Renal Impairment

Finerenone In Cardiorenal Syndrome :Clinical Trials at a Glance



https://doi.org/10.1007/s10741-025-10520-3

[a]Phase 3.

[b]Phase 2a (trial included an active comparator, spironolactone).

[c]Phase 2b.

Trial abbreviation definitions are in the full manuscript.

CKD chronic kidney disease; *EF* ejection fraction; *HF* heart failure; *HFmrEF* heart failure with mildly reduced ejection fraction; *HFpEF* heart failure with preserved ejection fraction; *HFrEF* heart failure with reduced ejection fraction; *PBO* placebo; *Pts*, patients; *T2D* type 2 diabetes

Phase II Finerenone Trials (ARTS Program)

https://doi.org/ 10.3390/jcm12196285

Studies	Duration	Sample Size	Study Design	Inclusion Criteria	Primary Outcome	Secondary Outcome	Conclusion
ARTS (Part A: finerenone vs. placebo; part B: finerenone vs. spironolactone or placebo) 2012 [28]	30 days	458	Multicenter, phase II study, with double-blind placebo and open-label spironolactone	• HFrEF (NYHA II-III, LVEF $\leq$ 40%) • Mild or moderate CKD (eGFR 60 to <90 (Part A) and 30–60 mL/min/ 1.73 m^2 (Part B))	Change in the serum potassium concentration vs. placebo	• Changes in the serum potassium concentration vs. spironolactone • Changes in the biomarkers of cardiac and kidney function or injury, eGFR (MDRD), and albuminuria	• Significantly smaller increases in potassium levels with finerenone than with spironolactone. • Finerenone was at least as effective as spironolactone in lowering NT-proBNP levels and albuminuria.
ARTS—HF (finerenone vs. eplerenone) 2016 [29]	90 days	1066	Randomized, double-blind, phase 2b multicenter study	• Worsening HF with HFrEF exacerbation and CKD and/or T2DM requiring hospitalization and intravenous diuretic therapy	Percent of patients with decrease of >30% of NT pro-BNP until day 90.	• All-cause death, CV hospitalizations, or worsening HF occurred least frequently in the finerenone 10 mg group versus the eplerenone group (hazard ratio 0.56; $p = 0.016$). • All-cause death ($p = 0.062$) and CV death ($p = 0.011$) occurred less frequently in the finerenone versus eplerenone groups.	• Finerenone is well tolerated and led to a $\geq$30% decrease in NT-proBNP levels similar to eplerenone. • All-cause death, CV hospitalization, or acute worsening HF was less common with finerenone than with eplerenone.
ARTS—DN (finerenone vs. placebo) 2015 [14]	90 days	823	Multicenter, double-blind, placebo controlled, phase II RCT	• CKD and T2DM receiving renin–angiotensin system inhibitors. • UACR $\geq$ 30 mg/g and eGFR > 30 mL/min/ 1.73 m^2	Change in UACR over 90 days vs. at baseline.	Hyperkalemia leading to study drug discontinuation was 2.1% in the 7.5 mg group, 0% in the 10 mg group, 3.2% in the 15 mg group, 1.7% in the 20 mg group, and 1.5% for placebo.	• UACR reduction was dose-dependent in the finerenone group compared to placebo, addition of finerenone compared with placebo resulted in improvement in the UACR. • Permanent drug discontinuation due to hyperkalemia not seen with placebo or finerenone 10 mg/day.

Phase III Clinical Trials of Finerenone

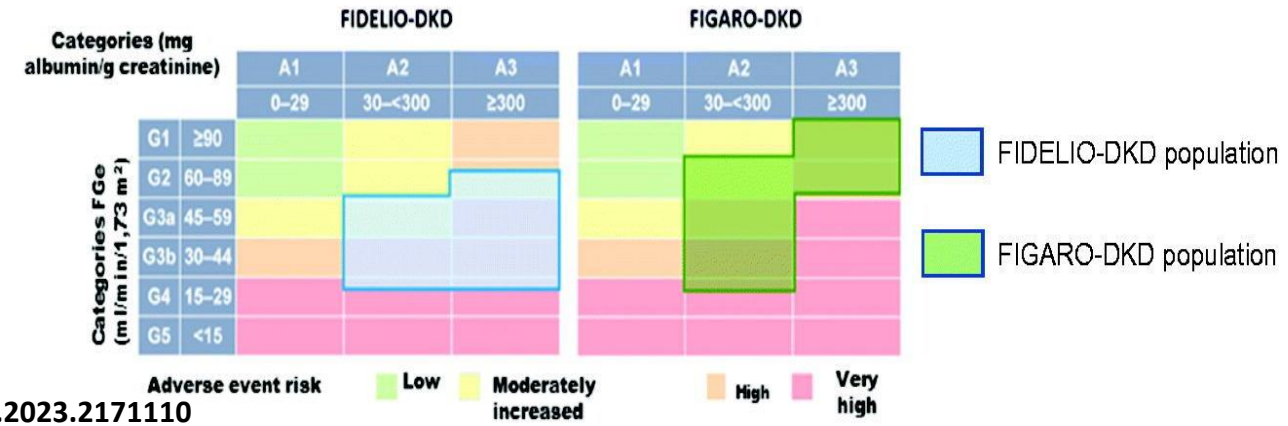
Design :
- Phase III clinical trial, multicenter, randomized, double blind, placebo controlled

	FIDELIO-DKD	FIGARO-DKD
Renal failure, sustained decrease eGFR ≥40% from basal levels or death renal cause	**Primary** outcome	Secondary outcome
CV death, non–fatal MI, non–fatal stroke or HF hospitalization	Secondary outcome	**Primary** outcome

Inclusion criteria :
- Age ≥18 years
- Type 2 diabetes
- Maximum tolerated doses of a RAAS inhibitor
- Serum potassium ≤4.8 mmol/L
- CKD:
  - **FIDELIO-DKD**: UACR 30–<300 mg/g, eGFR 25–<60 mL/min/1.73 m^2 and retinopathy, or UACR 300–5000 mg/g and eGFR 25–<75 mL/min/1.73 m^2
  - **FIGARO-DKD**: UACR 30–<300 mg/g and eGFR 25–90 mL/min/1.73 m^2, or UACR 300-5000 mg/g and eGFR ≥60 mL/min/1.73 m^2

FIDELIO-DKD
FIGARO-DKD

Exclusion criteria:
- Non-diabetes CKD
- Uncontrolled hypertension
- HbA1c >12%
- SBP <90mmHg
- Symptomatic chronic HFrEF
- Recent CV event
- Dialysis for acute renal damage
- Kidney transplant



https://doi.org/10.1080/07853890.2023.2171110

FIDELITY Trial

Pooled Analysis of FIDELIO-DKD + FIGARO-DKD

13,026 patients
T2DM + CKD + albuminuria
On maximal ACEi / ARB therapy

eGFR ≥25 mL/min/1.73m²
UACR 30–5000 mg/g

FINERENONE
n ≈ 6,513

R 1:1

PLACEBO
n ≈ 6,513

CARDIAC OUTCOMES

⬇ **14%** reduction in CV composite outcome (HR 0,86)

Composite included:
- CV death
- Nonfatal MI
- Nonfatal stroke
- HF hospitalization

⬇ **22%** reduction in HF hospitalization

RENAL OUTCOMES

⬇ **23%** reduction in kidney composite outcome (HR 0.77)

Composite included:
- Kidney failure
- Sustained ≥57% eGFR decline
- Renal death

⬇ **20%** reduction in ESKD

SAFETY

Hyperkalemia ↑
But treatment discontinuation remained relatively low

Finerenone discontinuation due to hyperkalemia:
1.7% vs 0.6%

KEY MESSAGE

FIDELITY established finerenone as a true cardiorenal protective therapy across the spectrum of diabetic CKD:

"One drug — dual organ protection"

Heart + Kidney

Summary of FINEARTS-HF

Objective: Assess impact of finerenone vs placebo in patients with HFmrEF and HFpEF on CV outcomes

6001 patients

Inclusion Criteria

- HFmrEF or HFpEF
- NYHA II-IV
- Structural heart disease or elevated natriuretic peptides

Exclusion Criteria

- eGFR < 25 ml/min/1.73 m^2
- K^+ > 5.0 mmol/L

3003 finerenone 10mg, 20mg or 40mg daily

2998 placebo

Results

Compared to placebo, patients who received finerenone had:

- ↓ risk of CVD and WHF events
- ↑ in KCCQ scores
- ↔ renal composite outcomes

From Diabetic CKD to Broader Cardiorenal Disease: The Next Chapter for Finerenone

It should be acknowledged that most of the current evidence for finerenone has been derived from patients with diabetic CKD, and robust data across the broader spectrum of cardiorenal syndrome—particularly in non-diabetic populations—remain limited.

However, this field is rapidly evolving. Ongoing and recently completed studies, such as FIND-CKD, is specifically evaluating finerenone in non-diabetic CKD, including patients with hypertensive nephropathy and chronic glomerular diseases such as IgA nephropathy. Early results are encouraging and suggest that the cardiorenal protective effects of finerenone may extend well beyond diabetic kidney disease

Design and baseline characteristics of the FIND-CKD trial testing finerenone in non-diabetic CKD

Focus was to describe the trial design and baseline characteristics of participants recruited to the FIND-CKD trial.

Methods

CKD without diabetes
eGFR ≥ 25 to < 90 mL/min/ 1.73 m² and UACR ≥ 200 to ≤ 3500 mg/g

Finerenone 10 or 20 mg vs. placebo

Primary endpoint:
Mean annual rate of change in eGFR from baseline to month 32

Secondary endpoint:
Cardiorenal, kidney, and cardiovascular composite outcomes

Results

N = 1584 randomised

Mean eGFR
46.7
mL/min/1.73 m²

Median UACR
818.9
mg/g

Cause of kidney disease
Hypertensive/ischaemic 29.0%
IgA nephropathy 26.3%
FSGS 13.6%

Cardiovascular history
Hypertension 88.1%
Atherosclerotic CVD 11.9%
Heart failure 2.2%

Concomitant medications
ACEi/ARB 99.8%
SGLT2 inhibitor 16.9%
Diuretic 17.8%

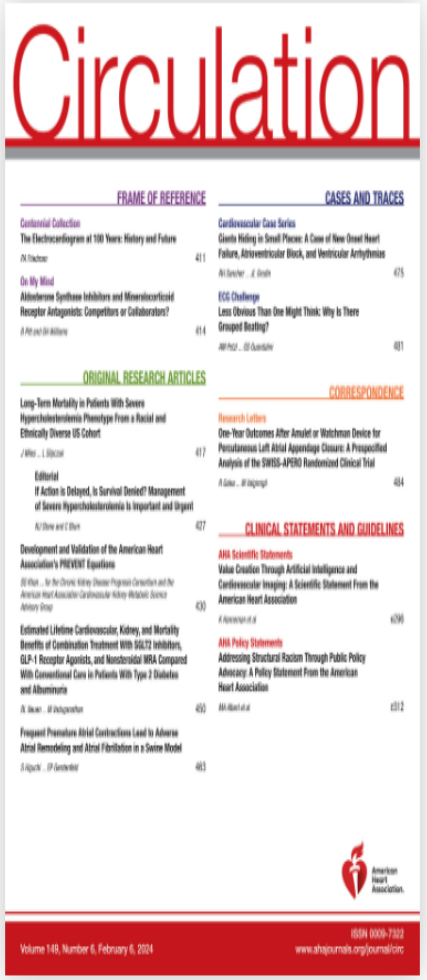
Heerspink, H. J. L. *et al.*
NDT (2024)
@NDTSocial

FIND-CKD is the first Phase 3 trial of finerenone in patients with CKD of non-diabetic aetiology and seeks to expand the role of finerenone for kidney protection beyond type 2 diabetes.

RESEARCH ARTICLE | Originally Published 12 November 2023 |

Estimated Lifetime Cardiovascular, Kidney, and Mortality Benefits of Combination Treatment With SGLT2 Inhibitors, GLP-1 Receptor Agonists, and Nonsteroidal MRA Compared With Conventional Care in Patients With Type 2 Diabetes and Albuminuria

Brendon L. Neuen, MBBS, MSc, PhD, Hiddo J.L. Heerspink, PhD, Priya Vart, PhD, Brian L. Claggett, PhD, Robert A. Fletcher, MSc, Clare Arnott, MBBS, PhD, Julianna de Oliveira Costa, PhD, ... SHOW ALL ... , and Muthiah Vaduganathan, MD, MPH



Clinical Perspective

What Is New?

- In this actuarial analysis using data from large-scale randomized outcome trials, combination treatment with SGLT2 inhibitors, GLP-1 receptor agonists and non-steroidal MRA in people with type 2 diabetes and at least moderately increased albuminuria was projected to afford substantial gains in cardiovascular, kidney and overall survival.
- Lifetime gains in event-free and overall survival were observed across the range of ages studied.

What Are the Clinical Implications?

- Implementation of the “4 pillars” of therapy for diabetes and chronic kidney disease – RAS blockade, SGLT2 inhibitors, GLP-1 receptor agonists and non-steroidal MRA – has the potential to offer major benefits to many individuals.
- Patients with type 2 diabetes at high cardiorenal risk should be prioritized for combination treatment with these “4 pillars” of guideline-directed medical therapy.

Finerenone in Predominantly Advanced CKD in Type 2 Diabetes With or Without SGLT-2i Therapy

ISN INTERNATIONAL SOCIETY OF NEPHROLOGY

Methods

Subgroup Analysis of FIDELIO-DKD

Placebo (with or without SGLT-2i)

VS

Finerenone (with or without SGLT-2i)

FIDELIO-DKD design

Global, multicenter, RCT, double blind, phase III trial (n = 5674)

eGFR 25-75 ml/min/1.73m^2

UACR 30-5000 mg/g

Type 2 diabetes

Finerenone VS Placebo

Findings

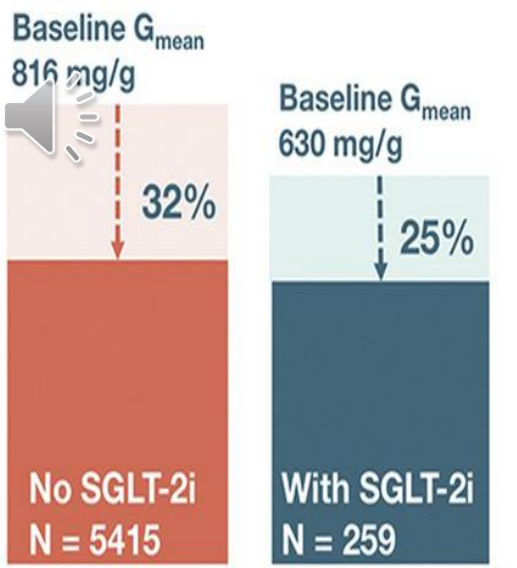
*Compared to those not treated with SGLT-2i

Finerenone with SGLT-2i use characteristics at baseline*

Higher eGFR

Lower UACR

UACR reduction (compared to placebo)



Compared to placebo, the kidney and CV benefits of Finerenone were consistent irrespective of SGLT2i use

Patients on SGLT-2i had fewer hyperkalemia events

SGLT-2i, sodium glucose cotransporter-2 inhibitor; RCT, randomized controlled trial; UACR, urine albumin creatinine ratio; CV, cardiovascular; G_{mean}, geometric mean

KI REPORTS
Kidney International Reports

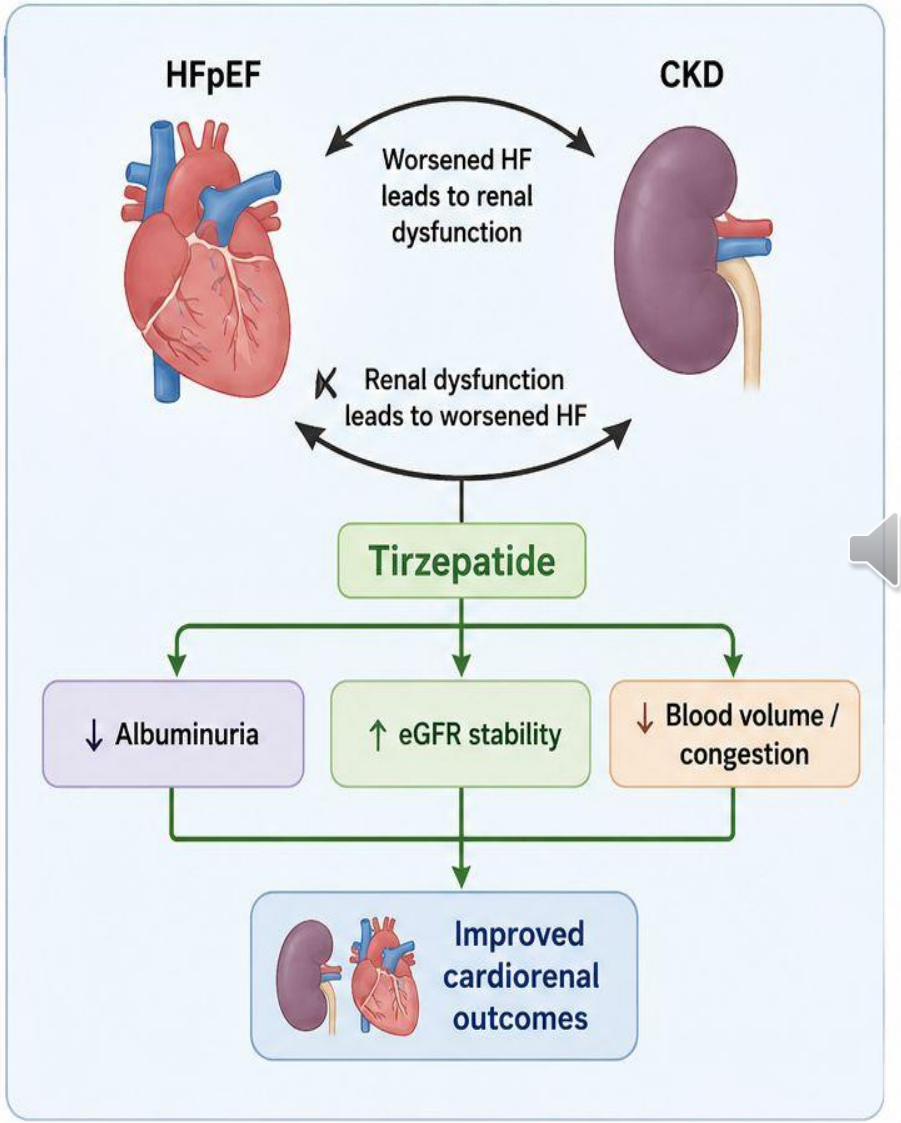
Rossing et al, 2022

Visual abstract by:
Sophia Ambruso, DO
@Sophia_kidney

Conclusion UACR improvement was observed with finerenone in patients with CKD and T2D already receiving SGLT-2i at baseline and benefits on kidney and cardiovascular outcomes appear consistent irrespective of SGLT-2i use.

GLP-1 Receptor Agonists in Cardiorenal Syndrome

Tirzepatide and Cardiorenal Benefits in HFpEF and CKD: *Insights from the SUMMIT Trial*



SUMMIT Trial

Solomon SD, McMurray JJV, Claggett B, et al. Tirzepatide in Patients with Heart Failure with Preserved Ejection Fraction and Obesity. *N Engl J Med.* 2024;391:109–121.

- **Population:** Patients with HFpEF and obesity (with or without type 2 diabetes)
- **Intervention:** Tirzepatide vs placebo on top of standard of care
- **Follow-up:** Median 104 weeks
- **Primary outcome:** Composite of cardiovascular death or worsening heart failure events

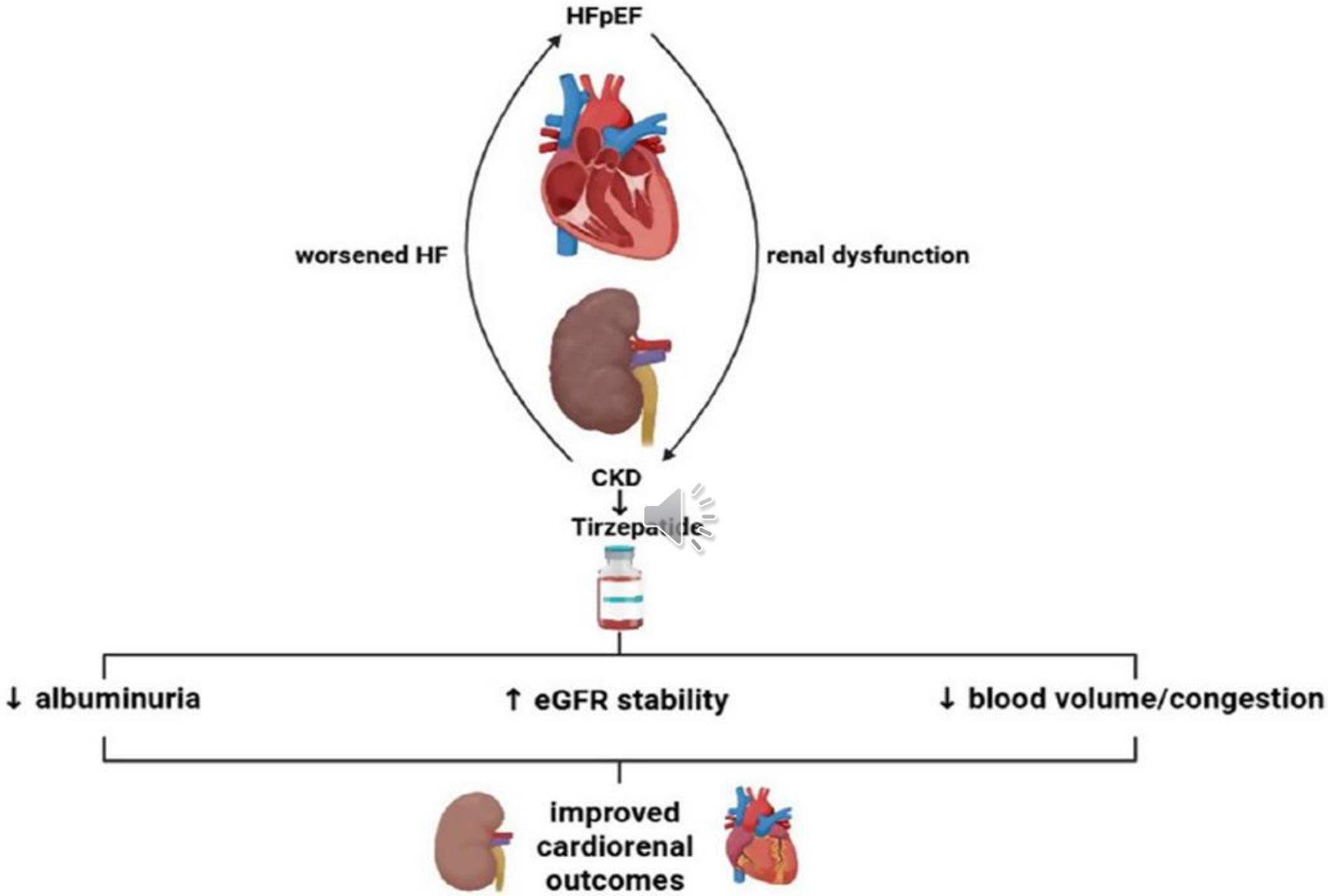
Key Findings Relevant to Cardiorenal Outcomes

- ✓ Tirzepatide reduced the risk of the primary cardiovascular outcome by 38% vs placebo (HR 0.62; 95% CI 0.41–0.95).
- ✓ Significant reductions in kidney outcomes, including worsening renal function and composite kidney events.
- ✓ Reduced albuminuria and favorable effects on eGFR trajectory.
- ✓ Reduced HF hospitalizations and improved symptoms.

→ SUMMIT supports the concept that tirzepatide provides **integrated cardiovascular and renal benefits in HFpEF**, beyond glycemic control and weight loss.

SUMMIT is the first large outcomes trial to demonstrate that tirzepatide improves both heart failure and kidney outcomes in patients with HFpEF and obesity, reinforcing the cardio-kidney-metabolic therapeutic paradigm.

Endocrinology, Diabetes & Metabolism, 2026; 9:e70152
https://doi.org/10.1002/edm2.70152



SUMMIT expanded the cardiorenal paradigm by showing that targeting obesity and metabolic inflammation with tirzepatide can improve heart failure outcomes, symptoms, and potentially kidney trajectories in HFpEF patients."

Semaglutide for CKD in Patients with Type 2 Diabetes: "FLOW"ing with the Semaglu"TIDE"

#NephJC

METHODS

International, double-blind, placebo-controlled
28 countries

Type 2 DM and CKD:
GFR 50-75 ml/min + ACR 300-5000 mg/g
or
GFR 25-<50 ml/min + ACR 100-5000 mg/g

Median follow-up, 3.4 years

	Major kidney disease events	Death from any causes	Adverse event leading to discontinuation
Placebo n = 1766	7.5 events per 100 patient-years	279(15.8%)	211(11.9%)
	HR 0.76 (95% CI, 0.66-0.88)	HR 0.80 (95% CI, 0.67-0.95)	
Semaglutide n = 1767	5.8 events per 100 patient-years	227(12.8%)	233(13.2%)

Major kidney disease events- kidney failure, ≥50% reduction in GFR, death from CV or kidney-related causes

HR= Hazard ratio

Reference: Perkovic,V et al. Effects of Semaglutide on Chronic Kidney Disease in Patients with Type 2 Diabetes. NEJM, May 2024.

VA by Anjana Gopal 𝕏@anjanagopal9

Conclusion: Semaglutide reduced the risk of clinically important kidney outcomes and death from cardiovascular causes in patients with type 2 diabetes and chronic kidney disease.

Take Home Massage

Cardiorenal syndrome is no longer managed by isolated heart or kidney strategies; it requires integrated multi-pathway therapy.

Modern cardiorenal management now extends beyond the traditional four pillars and includes SGLT2 inhibitors, RAAS/ARNI blockade, beta-blockers, mineralocorticoid receptor antagonism, and increasingly GLP-1 receptor agonists targeting the metabolic component of cardiorenal disease. Together, these therapies address congestion, maladaptive neurohormonal activation, inflammation, fibrosis, and cardiometabolic dysfunction simultaneously. Within this evolving framework, finerenone expands our ability to target the inflammatory–fibrotic axis and further refine comprehensive cardiorenal protection. The future of cardiorenal care is not organ-centered therapy, but continuum-centered therapy .

Thank You For Your Attention