CAMPUS Cuore SUMMIT

Napoli, 1-2 ottobre 2021
Hotel Excelsior

SGLT2 inibitori per il rischio evitabile di progressione dell'insufficienza renale nel paziente con diabete

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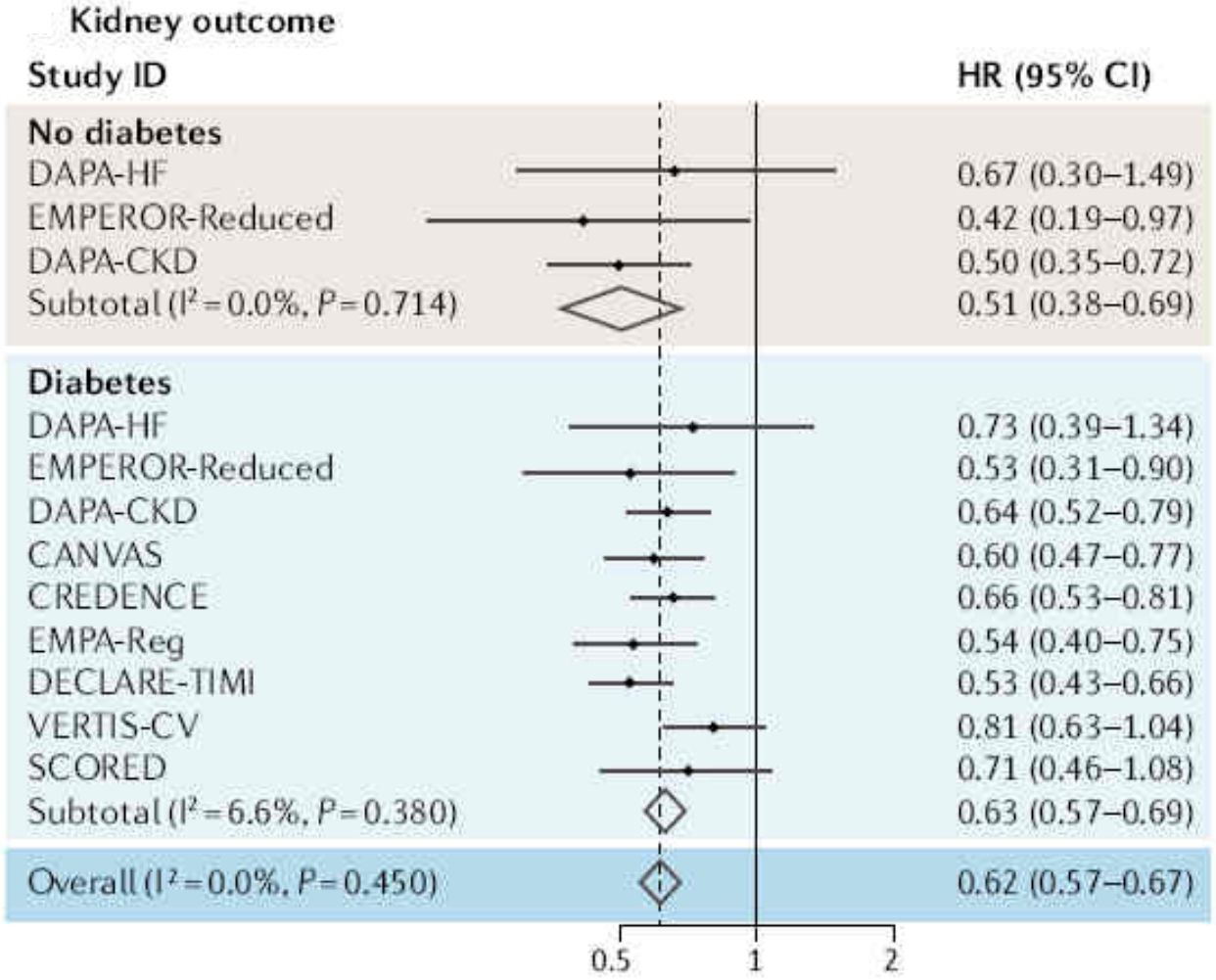
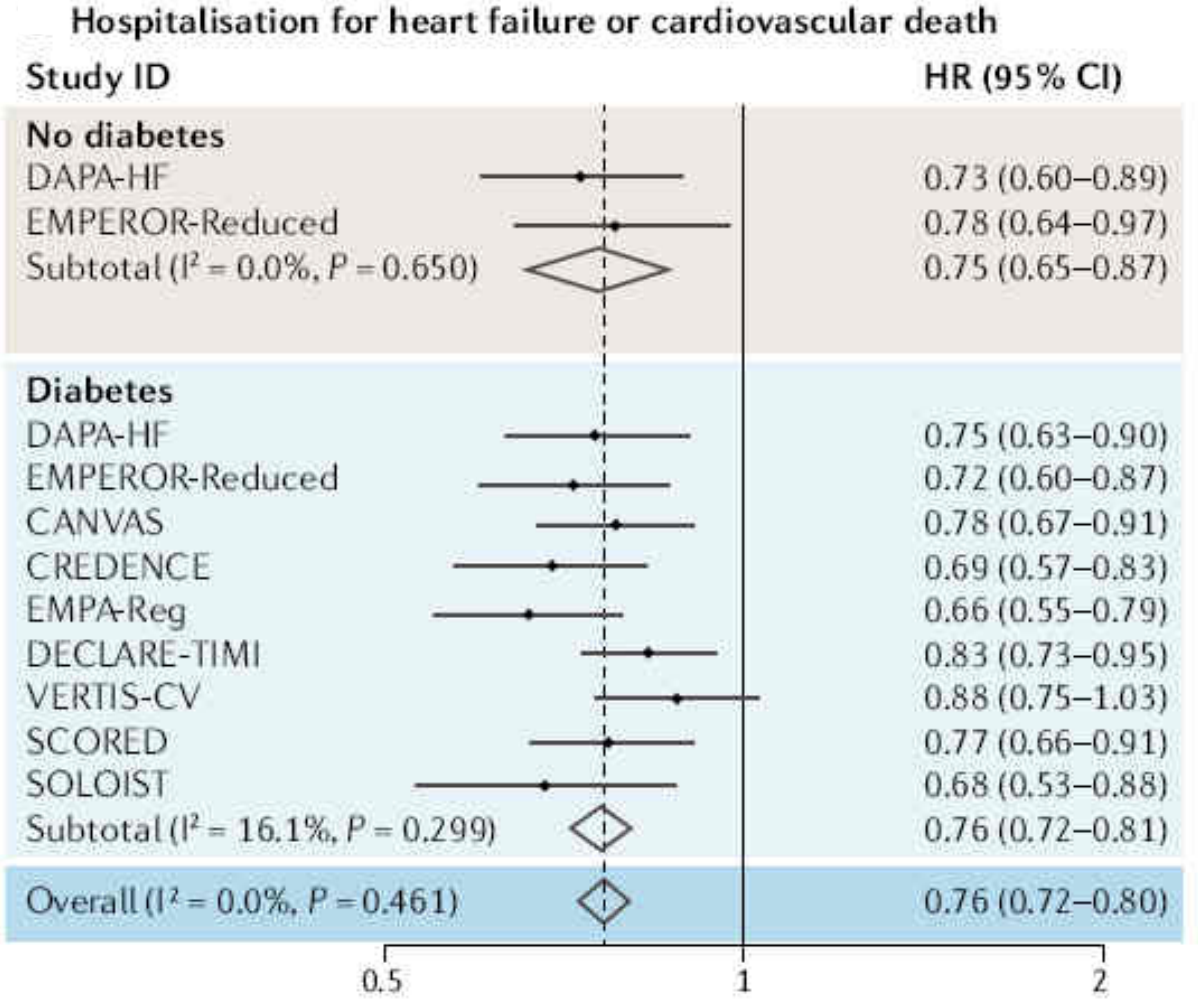
SGLT2 inhibition: "universal" cardionephroprotective efficacy





Kang and Jardine, Nat Rev Nephrol. 2021

SGLT2 inhibition: "universal" cardionephroprotective efficacy

Empagliflozin in Heart Failure with a Preserved Ejection Fraction

Similar in DM and non-DM patients !!!

- 5988 patients with class II–IV HF and EF >40%
- Mean eGFR 61 and eGFR <60 in 50%
- FU 26.2 months

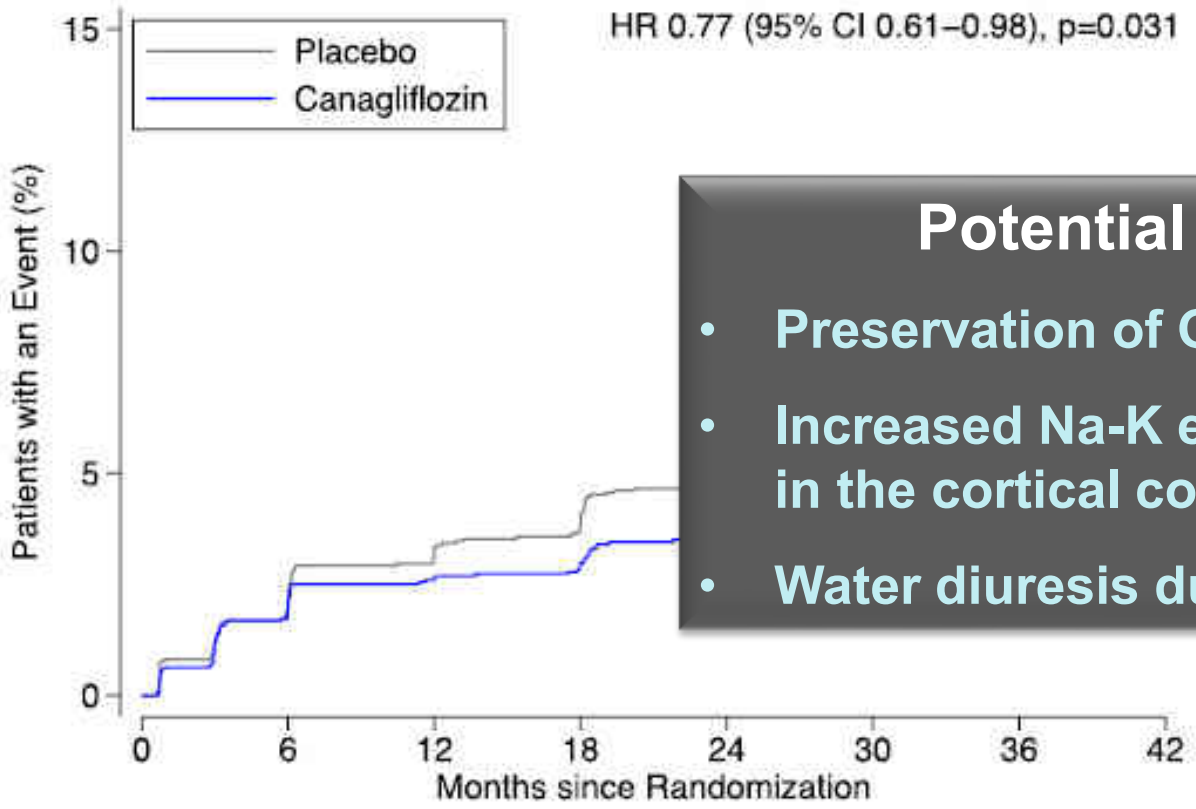
	Empagliflozin (N=2997)		Placebo (N=2991)		Hazard Ratio or Difference (95% CI)	P Value
		events per 100 patient-yr		*events per 100 patient-yr*		
Primary composite outcome — no. (%)	415 (13.8)	6.9	511 (17.1)	8.7	0.79 (0.69–0.90)	<0.001
Hospitalization for heart failure	259 (8.6)	4.3	352 (11.8)	6.0	0.71 (0.60–0.83)	
Cardiovascular death	219 (7.3)	3.4	244 (8.2)	3.8	0.91 (0.76–1.09)	
Secondary outcomes specified in hierarchical testing procedure						
Total no. of hospitalizations for heart failure	407	—	541	—	0.73 (0.61–0.88)	<0.001
eGFR (CKD-EPI) mean slope change per year — ml/min/1.73 m^2†	−1.25±0.11	—	−2.62±0.11	—	1.36 (1.06–1.66)	<0.001

Anker for EMPEROR-Preserved group, NEJM 27 Aug 2021

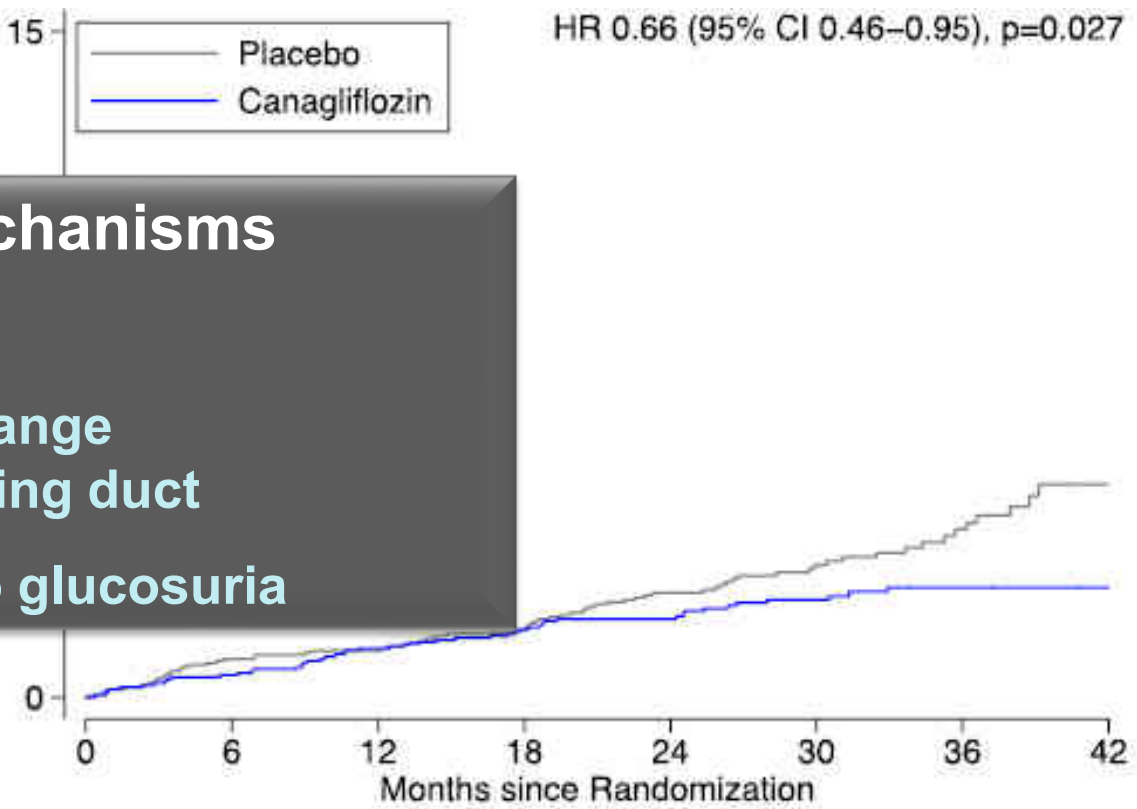
SGLT2-I and sK

Canagliflozin significantly reduces hyperkalemia in DKD patients

Serum potassium ≥6 mmol/L



Initiation of K binders

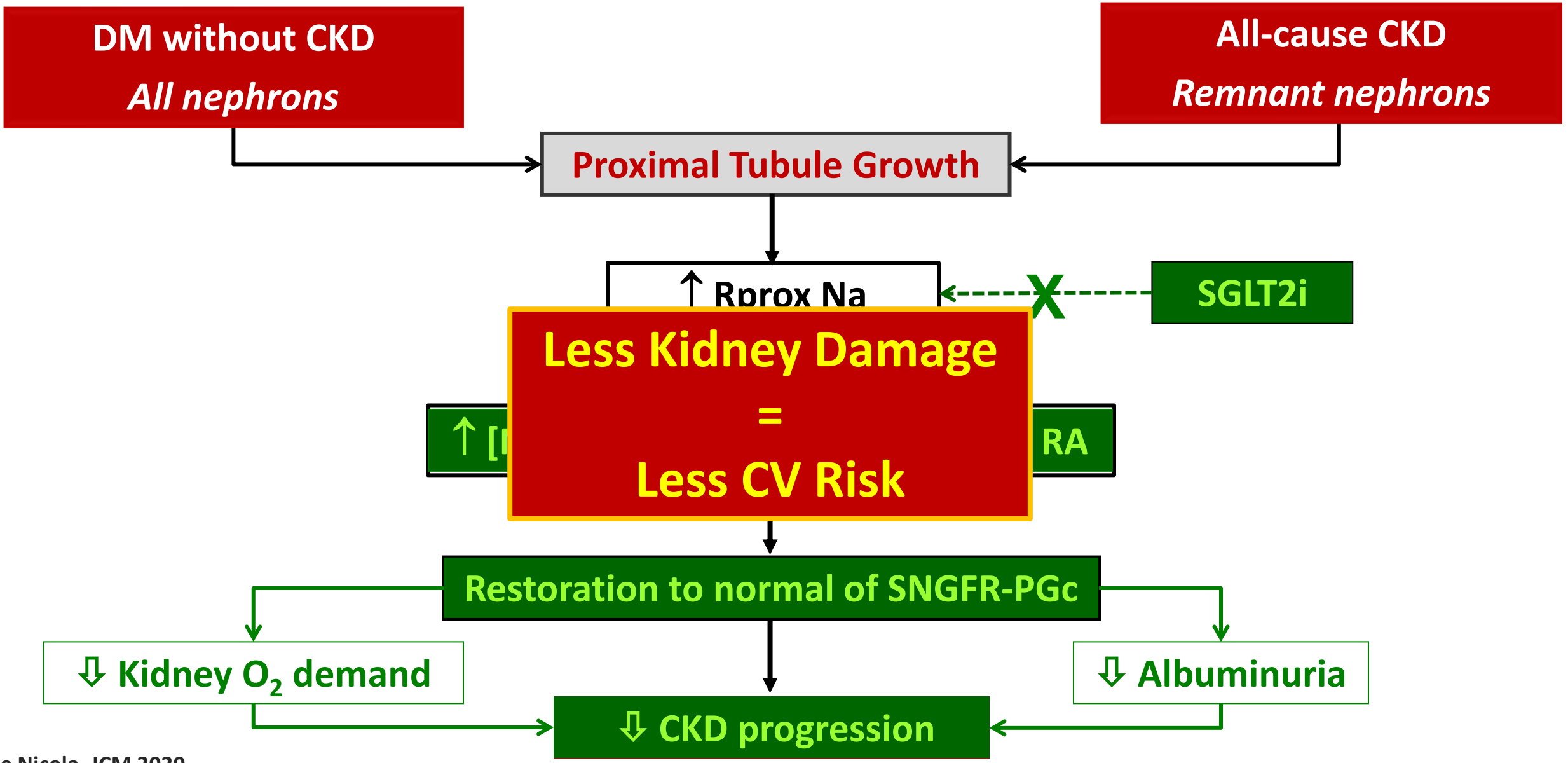


Potential Mechanisms

- Preservation of GFR
- Increased Na-K exchange in the cortical collecting duct
- Water diuresis due to glucosuria

Neuen BL…De Nicola L…Heerspink HL, for CREDENCE study group Eu Heart J 2021

Main postulated mechanism for SGLT2i-nephroprotection

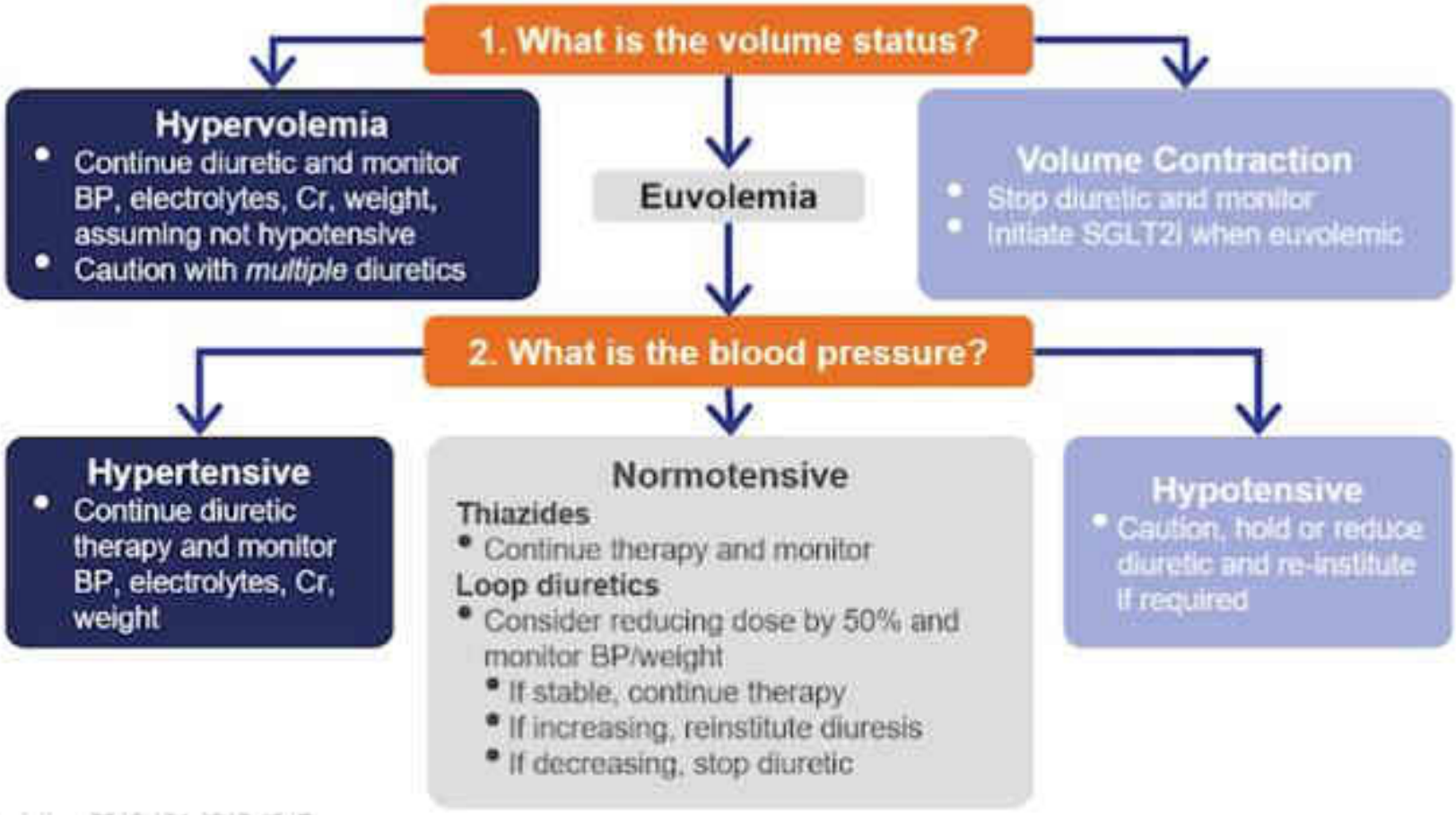


De Nicola, JCM 2020

PRACTICE POINTS

Prevent Volume Depletion

When adding an SGLT2i, continue diuretic and monitor



Adapted from Cherney and Udell, Circulation 2016

Network Meta-Analysis of Novel Glucose-Lowering Drugs on Risk of Acute Kidney Injury

Min Zhao,[1,2] Shusen Sun,[3,4,5] Zhenguang Huang,[2] Tiansheng Wang,[6] and Huilin Tang[7]

CJASN 16: 70–78, 2021.

CJASN
Clinical Journal of the American Society of Nephrology

Electronic databases
Pubmed
Embase
Cochrane CENTRAL

Up to September 2020

2 independent reviewers

Event-driven CV or kidney outcome trials

n = 18 trials
(Patients with Type 2 diabetes only)

n = 2 trials
(Patients with or without Type 2 diabetes)

18 trials

156,690
Patients with Type 2 diabetes only

2051
AKI events

Risk of AKI (vs placebo)

SGLT2 inhibitors	OR 0.76 (95% CI 0.66-0.88)
DPP-4 inhibitors	OR 1.12 (95% CI 0.93-1.35)
GLP-1R agonists	OR 0.96 (95% CI 0.83-1.11)

Risk of AKI (Comparisons between drugs)

SGLT2 inhibitors vs DPP-4 inhibitors	OR 0.68 (95% CI 0.54-0.86)
SGLT2 inhibitors vs GLP1-R agonists	OR 0.79 (95% CI 0.65-0.97)

CONCLUSIONS:

Current evidence indicates that SGLT2 Inhibitors have a lower risk of AKI than both DPP-4 inhibitors and GLP-1RAs

PRACTICE POINTS

Prevent /Treat Genital Infections

Genital infections affects up to 10% of women and 2-3% of men with type 2 DM

Li D et al., Diabetes Obes Metab 2017

Prevention

1. Suggest adequate water intake
2. Suggest proper genital hygiene (*pee, rinse, wipe*)

Intervention

- Intimate cleansing lotions

PRACTICE POINTS

Prevent Euglycemic Diabetic Ketoacidosis

- **EuDKA is rare: <0.5-0.1% of SGLT2-I treated diabetic patients**
- Due to imbalance between Insulin (↓) and Glucagon (↑) related to glycosuria and increased tubular ketone reabsorption secondary to volume depletion

Signs and Symptoms	Diagnostic Criteria	Risk factors
Asthenia Excessive thirst and urination Vomiting and abdominal pain Dehydration and hypotension Changes in mental status	SGLT2-I utilization Moderate hyperglycemia (less than 300 mg/dL) Metabolic acidosis with high anion gap Ketonemia and/or Ketonuria	Excessive alcohol consumption Type 1 DM or LADA Down-titration or discontinuation of insulin Low fasting C-peptide Reduced intake of calories Infections or intercurrent illness Surgery Acute cardiovascular events

LADA, latent autoimmune diabetes of adult.

- **TREATMENT: stop SGLT2-I in "*sick days*", normal saline, insulin iv (0.1 U/kg/hr),** bicarbonate iv if PH<7, glucose iv to prevent hypoglycemia

Nappi…De Nicola, Medicina 2019

Coming soon… SGT2-I for cardiologists and nephrologists

- Nephroprotection as class effect
- "Universal" efficacy (↓*glom hypertension*)
  - ✓ DM as non-DM CKD
  - ✓ HF as non-HF
  - ✓ Early as Late CKD (*stage 4*)
  - ✓ Proteinuric as non-Proteinuric
  - ✓ Diuretic/RAASI treated as untreated
- Monitor volaemia: Systolic BP and Body Weight (*downtitrate diuretic only if needed !*)
- Adequate hydration and intimate care
- Stop temporarily in "sick days"