

Congress Abstract

Morphological Basis of the Nephroprotective Effect of SGLT2 Inhibitors in Chronic Kidney Disease: A Systematic Review and Meta-Analysis

Anastassiya Ishkenova¹, Gaukhar Assanova¹, Kenzhekyz Manekenova¹, Talgat Omarov¹

¹NCJSC "Astana Medical University", Astana, Republic of Kazakhstan

Proceedings of Central Asian Congress of Nephrologists with International Participation, October 9-10, Aktau, Kazakhstan

Corresponding author's email:
an.pat.sme@gmail.com

Copyright: by the author(s).

License: A non-exclusive license by the publisher. Published by Australasia Publishing Group LLP (Astana, Kazakhstan) on behalf Kazakh Kidney Foundation.

Open Access: This article is an open access article distributed under the terms and conditions of the CC-BY Creative Commons Attribution license
<https://creativecommons.org/licenses/by/4.0>



ABSTRACT

Introduction: Chronic kidney disease (CKD) is characterized by progressive loss of kidney function driven by intraglomerular hypertension and hyperfiltration, podocyte and glomerular filtration barrier injury, tubular damage, and tubulointerstitial fibrosis. Sodium–glucose cotransporter 2 (SGLT2) inhibitors are increasingly recognized as nephroprotective agents whose effects extend beyond glycemic control to renal hemodynamic and structural mechanisms. The aim was to quantitatively assess the effect of SGLT2 inhibitors on the risk of CKD progression and to systematize evidence regarding the morphofunctional mechanisms underlying nephroprotection.

Methods: The quantitative meta-analysis included three major randomized controlled trials (RCTs): CREDENCE (canagliflozin; n=4,401), DAPA-CKD (dapagliflozin; n=4,304), and EMPA-KIDNEY (empagliflozin; n=6,609). Pooled treatment effects were calculated using a random-effects model according to the DerSimonian–Laird method after logarithmic transformation of hazard ratios (HRs). Ninety-five percent confidence intervals (95% CIs) were calculated from the reported trial estimates. Statistical heterogeneity was assessed using I^2 and Cochran's Q test. In parallel, experimental morphological evidence was systematically analyzed.

Results: SGLT2 inhibitors reduced the risk of the primary renal composite endpoint in individual trials: CREDENCE — HR 0.70 (95% CI 0.59–0.82), DAPA-CKD — HR 0.61 (95% CI 0.51–0.72), and EMPA-KIDNEY — HR 0.72 (95% CI 0.64–0.82). The pooled analysis yielded HR 0.68 (95% CI 0.62–0.75), corresponding to an approximately 32% relative reduction in risk. Between-study heterogeneity was low: $I^2=17.5\%$, Cochran's $Q=2.42$, and $\tau^2=0.0013$. An additional five-study analysis of renal-specific endpoints produced a pooled HR of 0.65 (95% CI 0.58–0.71), with $I^2=12.1\%$. Morphological evidence indicates attenuation of intraglomerular hyperfiltration, preservation of podocytes and components of the glomerular filtration barrier, reduced proximal tubular injury, and attenuation of tubulointerstitial fibrosis.

Conclusion: The meta-analysis of three major RCTs demonstrates a consistent reduction in the risk of CKD progression with SGLT2 inhibitor therapy: pooled HR 0.68 (95% CI 0.62–0.75), with low statistical heterogeneity ($I^2=17.5\%$). The nephroprotective effect is consistent with experimental morphological evidence demonstrating reduced hyperfiltration, preservation of the podocyte apparatus, and attenuation of tubular and tubulointerstitial injury and fibrosis. These findings support a multifactorial morphofunctional mechanism of SGLT2 inhibitor-mediated nephroprotection.

Keywords: SGLT2 Inhibitors; Chronic Kidney Disease; Nephroprotection; Renal Progression; Glomerular Hyperfiltration; Podocytes; Tubulointerstitial Fibrosis; Systematic Review; Meta-Analysis

Table 1. Main results of the quantitative meta-analysis

Study	Drug	n	HR (95% CI)	Endpoint
CRENCE	Canagliflozin	4,401	0.70 (0.59–0.82)	Primary renal composite endpoint
DAPA-CKD	Dapagliflozin	4,304	0.61 (0.51–0.72)	Primary renal composite endpoint
EMPA-KIDNEY	Empagliflozin	6,609	0.72 (0.64–0.82)	Primary renal composite endpoint
Pooled effect	SGLT2 inhibitors	15,314	0.68 (0.62–0.75)	Random-effects model

Data on the impact of SGLT2 inhibitors on the risk of CKD progression are presented in Figure 1.

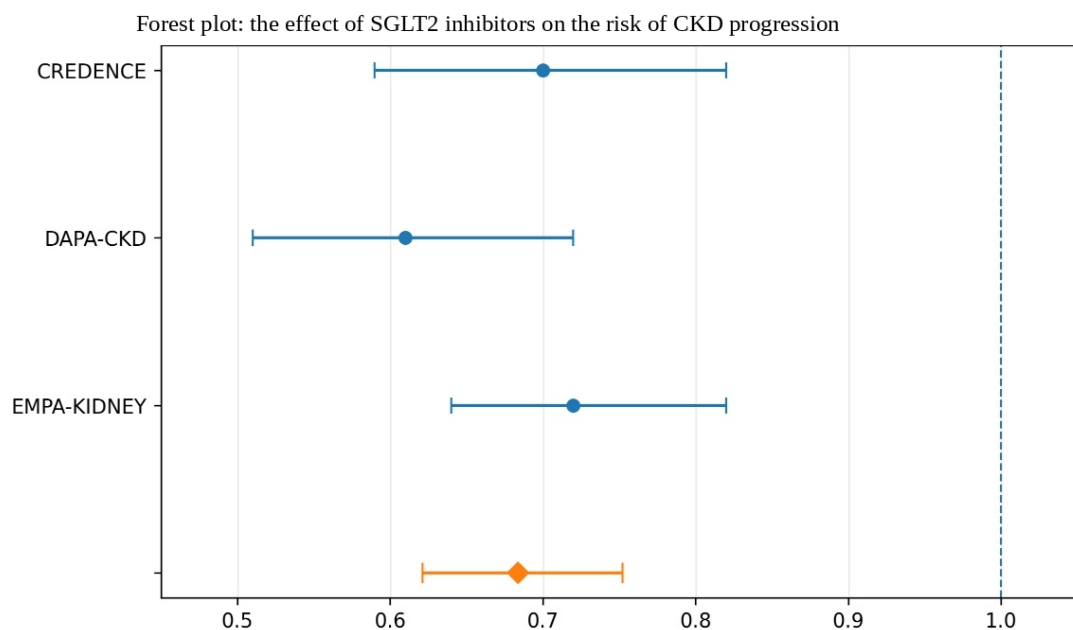


Figure 1: The primary quantitative analysis was based on three trials with comparable renal composite endpoints. The five-study analysis should be interpreted as an additional exploratory analysis because of differences in endpoint definitions and study populations/designs.