



# Short-Term Effectiveness and Safety of Sodium-Glucose Cotransporter-2 Inhibitors in Type 2 Diabetic Patients with Renal Transplantation: A Retrospective Study

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## Abstract

**Introduction** Sodium-glucose cotransporter-2 inhibitors (SGLT2i) provide robust cardio-renal benefits in the general population with type 2 diabetes mellitus (T2DM) and chronic kidney disease (CKD). However, kidney transplant recipients (KTRs) have been excluded from pivotal randomized trials, creating a critical data gap regarding the short-term efficacy and safety of SGLT2i in this uniquely vulnerable, high-risk group. This study investigated the short-term effectiveness of SGLT2i in glycemic management and their safety in relation to allograft function in Vietnamese KTRs with T2DM.

**Methods** This retrospective study included 281 KTRs with T2DM at Cho Ray Hospital, Vietnam, divided into an SGLT2i-treated group (n = 140) and a non-SGLT2i group (n = 141). Primary outcomes included changes in fasting plasma glucose (FPG), estimated glomerular filtration rate (eGFR), and creatinine levels measured at baseline and after 12 months. Potential adverse events (urinary tract infection, yeast infection, and hypotension) were also monitored.

**Results** Over the 12-month period, the SGLT2i group showed a significant reduction in FPG, an effect not observed in the control group. Critically, SGLT2i use was associated with the preservation of allograft function, showing stable eGFR and creatinine levels. Furthermore, no defined adverse events were observed in the treatment group.

**Conclusion** SGLT2i are effective in achieving short-term glycemic control and demonstrate a reassuring safety profile regarding allograft function in this cohort of Vietnamese KTRs. These findings support the cautious, individualized integration of SGLT2i into the care regimen for stable KTRs with T2DM, while underscoring the urgent need for long-term randomized controlled trials to validate definitive renoprotective outcomes.

**Keywords** Renal transplantation · Sodium glucose cotransporter-2 inhibitor · Diabetes mellitus · Retrospective study

## 1 Introduction

Sodium-glucose cotransporter-2 inhibitors (SGLT2i) are a class of drugs approved primarily for type 2 diabetes mellitus (T2DM) treatment by inhibiting glucose reabsorption from the proximal renal tubule [1]. In cardiovascular outcome trials, SGLT2i have demonstrated superiority over a placebo in cardio-renal protection, leading to updated guidelines

for managing T2DM [2–5]. Furthermore, SGLT2i has been shown to reduce cardiovascular and renal composite outcomes in patients with chronic kidney disease (CKD) [6–8]. However, patients who have undergone renal transplantation have been excluded from these large randomized control trials, and so the short-term efficacy in glycemic management and even long-term efficacy in cardiovascular and renal protection of SGLT2i in these patients remains undetermined. Recently, observational studies have shown that SGLT2i are generally safe and efficacious in patients with renal transplants, and ongoing clinical trials aim to answer questions about cardiovascular and renal protection by SGLT2i in these patients [9, 10]. This study set out to investigate the short-term efficacy of SGLT2i for glycemic management and the safety of SGLT2i in terms of kidney function changes in Vietnamese patients with renal transplants.

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## 2 Materials and Methods

### 2.1 Study Population and Design

This is a retrospective study conducted at Cho Ray Hospital, Ho Chi Minh City, Vietnam. The inclusion criteria were patients diagnosed with T2DM who had undergone their first kidney transplant; these patients were divided into two groups: one was continuously managed with SGLT2i for at least 1 year, and the other was not treated with SGLT2i.

Patient characteristics such as age, gender, body mass index (BMI), duration of hemodialysis, and time after renal transplant were collected. Paraclinical information, including creatinine level, fasting plasma glucose (FPG), and HbA1c, was recorded at baseline and after 6 and 12 months after initiation of SGLT2i. Potential adverse events of using SGLT2i were urinary tract infection, yeast infection, hypotension, hospitalization or emergency visit, and any event leading to SGLT2i discontinuation. These side effects were identified based on routine history taking and urinary analyses. Allograft function was assessed by the changes of creatinine levels and estimated glomerular filtration rate (eGFR) over 6 and 12 months. eGFR was calculated using CKD-EBI 2021 formula. All patient data were obtained from the medical records from the hospital system with the approval of the Ethical Committee of Cho Ray Hospital (Approval number 15–25/GCN-HDDD).

### 2.2 Statistical Analysis

Depending on their distribution, continuous variables were expressed either as mean  $\pm$  standard deviation or median (interquartile range). Categorical variables were expressed as counts (percentages). Student t-tests, Mann–Whitney tests, Chi-squared, and Fisher's exact tests were used to examine the differences between the compared groups. ANOVA tests were used to compare the differences between multiple means. ANCOVA analyses with covariate adjustment were used to compare means between two treatment groups. A two-tailed  $p$ -value  $< 0.05$  was considered statistically significant. All the analyses were performed using SPSS computer software version 22.0 (IBM Corp) (Table 1).

## 3 Results

A total of 281 T2DM patients after kidney transplants were identified. The median age of the studied population was 55, and 68.3% were female. The median duration of hemodialysis was 1 year and the median time after renal transplantation was 8 years. There were significant

differences between the patient group with and without SGLT2i in terms of BMI, creatinine, and FPG levels at baseline. The patients treated with SGLT2i had higher BMI, lower creatinine levels, and higher FPG levels.

One year after treatment, none of the defined adverse effects were observed in patients using SGLT2i within the study population. The use of SGLT2i resulted in a notable reduction in glucose levels throughout the course of treatment, an improvement that was not observed in patients who did not receive SGLT2i (Table 2). Regarding kidney safety, both eGFR and creatinine levels remained stable over the course of 1 year (Table 3). ANCOVA analyses adjusting for covariates such as baseline BMI, FPG, and creatinine levels showed that there were no statistical differences in FPG and creatinine levels at month 6 and month 12 between the two groups with and without SGLT2i treatment (Table 4).

## 4 Discussion

SGLT2i are a game-changer in the therapeutic landscape for T2DM due to their robust glucose-lowering capacity together with substantial cardio-renal protective benefits demonstrated in large-scale cardiovascular outcome trials [3–5]. Although kidney transplant recipients (KTRs) with T2DM are at increased risk for cardiovascular mortality, infection, and accelerated allograft failure, they have been routinely excluded from foundational trials. This exclusion has resulted in a significant clinical gap regarding the efficacy and safety of SGLT2i in this uniquely vulnerable population.

This retrospective study, investigating the short-term use of SGLT2i such as empagliflozin and dapagliflozin in Vietnamese KTRs with T2DM, addresses this critical data deficiency. The findings confirm the effectiveness of SGLT2i in glycemic management and provide encouraging short-term safety data concerning allograft function and adverse event profiles, serving as an important contribution, particularly given the focus on an Asian cohort with distinct anthropometric characteristics.

The primary findings support the clinical utility of SGLT2i in glycemic control. Specifically, the SGLT2i group demonstrated a significant reduction in FPG. This glucose-lowering effect is consistent with the established mechanism of SGLT2 inhibition, which increases urinary glucose excretion independent of insulin action [11]. The magnitude of this glycemic improvement aligns with the results of previous smaller-scale observational studies and the randomized, placebo-controlled trial of empagliflozin in KTRs, which similarly reported significant reductions in HbA1c and improved metabolic profiles [12].

**Table 1** Baseline characteristics of the studied population

Characteristics	Total (n=281)	SGLT2i use		p-value
		Yes (n=140)	No (n=141)	
Age (years)	55.0	56.0	55.0	0.366
Median (IQR)	(44.0–64.0)	(47.0–63.0)	(42.0–64.0)	
Gender				0.548
N (%)				
Female	192 (68.3%)	98 (70.0%)	94 (66.7%)	
Male	89 (31.7%)	42 (30.0%)	47 (33.3%)	
Duration of hemodialysis (years)	1.0	1.00	1.0	0.749
Median (IQR)	(1.0–2.0)	(1.0–2.0)	(1.0–2.0)	
SGLT2i use N (%)				
Empagliflozin	–	59 (42.1)	–	–
Dapagliflozin	–	81 (57.9)	–	–
Time since renal transplant (years)	8.0	9.00	7.0	0.121
Median (IQR)	(6.0–10.0)	(6.8–10.0)	(5.0–10.0)	
BMI (kg/m <sup>2</sup> )	22.5 ± 3.0	23.4 ± 2.8	21.7 ± 2.9	<0.001
Mean ± SD				
Creatinine (mg/dL)	1.3 ± 0.7	1.2 ± 0.4	1.4 ± 0.9	0.021
Mean ± SD				
eGFR (ml/min/1.73m <sup>2</sup> )	68.5 ± 22.2	70.5 ± 19.8	66.4 ± 24.2	0.058
Mean ± SD				
Glucose (mg/dL)	127.3 ± 50.2	140.4 ± 59.7	114.3 ± 34.0	<0.001
Mean ± SD				
HbA1c (%)	7.7	7.7	7.7	0.356
Median (IQR)	(6.7–9.3)	(6.8–9.4)	(6.6–8.3)	
Antidiabetic agent use (N%)	172 (61.2)	90 (64.3)	82 (58.2)	0.328
Metformin	25 (8.9)	10 (7.1)	15 (10.6)	0.402
Sulfonylurea	150 (53.4)	76 (54.3)	74 (52.5)	0.811
DDP4i	103 (36.7)	49 (35.0)	54 (38.3)	0.621
Insulin				
Tacrolimus use N (%)	192 (68.3)	95 (67.9)	97 (68.8)	0.866
Cyclosporine use N (%)	88 (31.3)	45 (32.1)	43 (30.5)	0.766

BMI: body mass index, eGFR: estimated glomerular filtration rate, SGLT2i: sodium-glucose cotransporter-2 inhibitor

**Table 2** Changes in FPG in the study population

FPG (mg/dL)	Baseline	Month 6	Month 12	p-value
Total study	127.36 ± 50.21	116.79 ± 39.24	120.98 ± 36.40	0.012
With SGLT2i	140.46 ± 59.75	124.69 ± 44.28	127.71 ± 40.27	0.017
Without SGLT2i	114.36 ± 34.00	108.95 ± 31.77	114.30 ± 30.81	0.271

FPG: fasting plasma glucose, SGLT2i: sodium-glucose cotransporter-2 inhibitor

**Table 3** Changes in creatinine level and eGFR in the studied population

Creatinine level (mg/dL)	Baseline	Month 6	Month 12	p-value
Total study	1.32 ± 0.72	1.29 ± 0.61	1.34 ± 0.77	0.746
With SGLT2i	1.22 ± 0.38	1.20 ± 0.38	1.19 ± 0.40	0.906
Without SGLT2i	1.41 ± 0.94	1.38 ± 0.77	1.47 ± 0.99	0.667
eGFR (ml/min/1.73m <sup>2</sup> )	Baseline	Month 6	Month 12	p-value
Total study	68.48 ± 22.17	69.34 ± 22.76	68.77 ± 23.30	0.901
With SGLT2i	70.58 ± 19.74	71.40 ± 19.60	72.38 ± 21.06	0.758
Without SGLT2i	66.40 ± 24.23	67.29 ± 25.42	65.17 ± 24.90	0.772

eGFR: estimated glomerular filtration rate, SGLT2i: sodium-glucose cotransporter-2 inhibitor

**Table 4** ANCOVA analyses of FPG and creatinine levels adjusting for baseline BMI, FPG and creatinine levels

	Estimated marginal means of FPG level				Estimated marginal means of creatinine level			
	Month 6	p-value	Month 12	p-value	Month 6	p-value	Month 12	p-value
With SGLT2i	121.26 ± 3.33	0.072	124.92 ± 3.12	0.089	1.28 ± 0.04	0.635	1.27 ± 0.05	0.09
Without SGLT2i	112.34 ± 3.33		117.07 ± 3.11		1.30 ± 0.04		1.40 ± 0.05	

BMI: body mass index, FPG: fasting plasma glucose, SGLT2i: sodium-glucose cotransporter-2 inhibitor

A crucial consideration here is the typical anthropometric profile of the Vietnamese cohort studied. The BMI was relatively low at baseline, which differs from the higher BMI levels typically seen in major cardiovascular outcome trials. The demonstration of clinically meaningful FPG reduction confirms that the SGLT2i mechanism is effective in KTRs presenting with the “lean diabetes” phenotype common in many East Asian populations [13]. This result validates the use of SGLT2i across the different ethnic and anthropometric spectrums prevalent in Vietnam and Southeast Asia. Furthermore, the inherent tendency of SGLT2i to induce weight loss, as documented in other KTR studies, offers a critical ancillary benefit, addressing the weight gain frequently associated with chronic immunosuppressive regimens in the transplant setting. Another interesting point of the study was the predominance of female KTR, as this is different from other kidney transplantation studies. The reason behind this result was unclear and it should be cautious when generalizing this observation to other populations.

A primary goal of this study was to assess the short-term safety of SGLT2i concerning allograft function. The data presented are highly encouraging, demonstrating the preservation of eGFR in the SGLT2i group over the 12-month treatment period. Both the treated and untreated groups maintained stable eGFR trajectories, suggesting that SGLT2i use did not precipitate an acute or subacute deterioration of allograft function within 1 year.

We acknowledged the absence of urine albumin-to-creatinine ratio (UACR) measurements as a significant limitation. This omission substantially limits the ability of the study to fully quantify the degree of renoprotective efficacy achieved by SGLT2i in this cohort. UACR reduction serves as a critical, robust intermediate endpoint that precedes and correlates strongly with decreased risks of major adverse cardiovascular events and the progression of kidney failure in patients with CKD and T2DM [14]. The mechanical reduction in intraglomerular pressure resulting from SGLT2 inhibition is specifically expected to translate into reduced albuminuria [15]. Future research should routinely incorporate UACR measurement to confirm that the hemodynamic stabilization suggested by eGFR data is indeed coupled with the expected anti-proteinuric and subsequent anti-fibrotic effects, thereby validating the full cardio-renal protective benefit of SGLT2i in this patient group. Another major

limitation of this study was the lack of HbA1c data at 6 and 12 month. This limitation strongly affects the conclusion regarding glycemic control effectiveness.

A central concern in the use of SGLT2i in KTRs—who are chronically immunosuppressed—is the increased risk of infections, particularly urinary tract infections (UTIs) and genital mycotic infections (GMIs) [16]. This study reports a favorable short-term safety profile in the SGLT2i group over the 12-month period, noting zero defined adverse events, including UTI, yeast infection, and clinically significant hypotension. While GMI is a recognized class effect in the general T2DM population, several transplant-specific studies, particularly those involving Asian cohorts, have consistently reported a low or non-increased risk of both UTI and GMI in KTRs compared to control groups [13, 15]. The reported zero incidence of these events must be interpreted cautiously, as retrospective chart reviews may fail to capture mild, transient infections or instances of hypotension managed without intervention or hospitalization. Nevertheless, the absence of major events requiring hospitalization—such as severe pyelonephritis, debilitating hypovolemia leading to acute kidney injury, or diabetic ketoacidosis—relatively confirms the short-term clinical feasibility and safety of SGLT2i in this stable, immunosuppressed cohort [16]. This finding offers significant reassurance to clinicians considering SGLT2i therapy in KTRs.

Despite the overwhelming evidence of cardio-renal benefit in the general CKD and T2DM populations, current clinical practice guidelines, such as the Kidney Disease: Improving Global Outcomes (KDIGO) 2022 Clinical Practice Guideline, explicitly state that SGLT2i use is not yet recommended for KTRs [17]. This exclusion is based solely on the historical lack of dedicated, sufficiently large randomized outcome trials focused on this specific cohort.

The accumulating evidence from observational studies, including the present analysis of Vietnamese KTRs, consistently demonstrates reliable glycemic efficacy, stable allograft function, and a short-term safety profile [10]. Given the exceptionally high morbidity and mortality burden faced by KTRs with T2DM, reliance solely on the historical exclusion criteria becomes increasingly difficult to justify clinically. The collective data now support the cautious, off-label integration of SGLT2i into the therapeutic regimen

for selected stable KTRs, particularly those with higher metabolic needs (elevated FPG, higher BMI) and robust baseline allograft function. To overcome methodological bias inherent in retrospective analyses and elevate SGLT2i to guideline-directed standard therapy for KTRs, future research must shift focus from short-term safety verification to definitive, long-term outcome validation [10].

The primary mandate is the urgent completion of ongoing randomized controlled trials, such as studies examining dapagliflozin in KTRs [18]. These trials must define primary endpoints that are clearly related to hard outcomes in kidney disease progression, including sustained eGFR decline, requirement for chronic dialysis, allograft loss, or cardiovascular death.

## 5 Conclusions

This retrospective study from a Vietnamese cohort provides short-term evidence reinforcing the effectiveness and safety of SGLT2i in KTRs with T2DM. The analysis confirms short-term glycemic improvement and demonstrates the stability of allograft function over 12 months. The study also reports an encouraging safety profile with zero observed adverse events related to UTI, yeast infection, or hypotension, echoing the safety observed in other Asian and international cohorts.

While the data support the cautious integration of SGLT2i into the care of stable KTRs, the inherent limitations of retrospective design and the critical absence of UACR measurements necessitate restraint regarding claims of definitive long-term renoprotection. The findings underscore the urgent need for ongoing, large-scale randomized controlled trials that rigorously measure hard clinical endpoints and validated intermediate markers like UACR. Until such data are available, the present evidence justifies the careful, individualized use of SGLT2i as an invaluable therapeutic tool for diabetic KTRs.

**Author Contributions** HP and MD designed the research study. AL collected the data. HP and MD analyzed the data. HP and MD wrote the manuscript.

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**Data Availability** Data supporting the findings of this study are available from the corresponding author [MD] on request. Raw data were generated at Cho Ray Hospital, Ho Chi Minh City, Vietnam.

## Declarations

**Conflict of interest** The authors declare no competing interests.

**Ethical Approval** This study was approved by the Ethics Committee for Medical Research of Cho Ray Hospital (approval number 15–25/GCN-HDDD).

**Human and Animal Participants** Patients and/or the public were not involved in the design, conduct, reporting, or dissemination plans of this research.

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