The Efficacy and Safety of SGLT2 Inhibitor in Diabetic Kidney Transplant Recipients

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Supplemental Digital Content Table of Contents

Table S1. Baseline characteristics before and after propensity score matching

Table S2. Antidiabetic and immunosuppressive medication history in propensity score-matched groups

Table S3. Serial comparisons of mean eGFR between the dipper and nondipper groups among SGLT2i users

Table S4. Multiple comparisons of mean eGFR changes from baseline in each dipper and nondipper group

Table S5. Baseline characteristics between the dipper and nondipper groups

Table S6. The incidences of urinary tract infection

Figure S1. Kaplan–Meier curves for the primary composite outcome and individual components in propensity score-matched group. (A) Primary composite outcome of all-cause mortality, death-censored graft failure, or serum creatinine doubling. (B) All-cause mortality. (C) Death-censored graft failure. (D) Serum creatinine doubling.

Table S1. Baseline characteristics before and after propensity score matching

	Before matching			After matching		
	SGLT2i users (n = 210)	SGLT2i nonusers (n = 1607)	*P*	SGLT2i users (n = 202)	SGLT2i nonusers (n = 554)	*P*
Age, y	51.5 ± 10.9	53.1 ± 10.0	0.036	51.8 ± 10.8	52.4 ± 9.3	0.483
Sex, male, n (%)	145 (70.0)	1084 (68.3)	0.659	142 (70.3)	384 (69.3)	0.865
Etiology of ESKD, DM, n (%)	137 (66.2)	1092 (68.8)	0.501	134 (66.3)	372 (67.1)	0.903
Pretransplant comorbidities, n (%)						
Hypertension	171 (82.6)	1228 (77.3)	0.102	166 (82.2)	452 (81.6)	0.937
Dyslipidemia	12 (5.7)	126 (7.8)	0.339	12 (5.8)	44 (7.1)	0.621
Donor type, n (%)			0.031			0.837
Deceased	46 (22.2)	472 (29.7)		46 (22.8)	132 (23.8)	
Living	161 (77.8)	1116 (70.3)		156 (77.2)	422 (76.2)	
ABO incompatibility, n (%)	36 (17.4)	230 (14.5)	0.316	35 (17.3)	93 (16.8)	0.984
HbA1c, 1-yr AUC, %	7.4 ± 1.3	7.3 ± 1.2	0.200	7.4 ± 1.3	7.4 ± 1.2	0.665
eGFR at 3 months after KT, mL/min/1.73 m^2	66.7 ± 17.5	68.1 ± 20.3	0.318	66.8 ± 17.6	67.7 ± 18.7	0.558
Metformin usage, n (%)	184 (88.9)	912 (57.4)	<0.001	179 (88.6)	489 (88.3)	0.997
Acute rejection, n (%)	81 (39.1)	424 (26.7)	<0.001	76 (37.6)	168 (30.3)	0.070
ACEi or ARB usage, n (%)	103 (49.8)	543 (34.2)	<0.001	98 (48.5)	249 (44.9)	0.430

SGLT2i, sodium-glucose cotransporter 2 inhibitors; ESKD, end-stage kidney disease; DM, diabetes mellitus; AUC, area under the curve; eGFR, estimated glomerular filtration rate; KT, kidney transplantation; ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker.

Table S2. Antidiabetic and immunosuppressive medication history in propensity score-matched groups

Variables	Total (n = 756)	SGLT2i users (n = 202)	SGLT2i nonusers (n = 554)	*P*
Antidiabetic medication after KT				
Metformin, n (%)	668 (88.4)	179 (88.6)	489 (88.3)	0.997
Duration, days	1301.1 ± 1016.4	1154.5 ± 970.6	1355.9 ± 1028.6	0.002
Sulfonylurea, n (%)	328 (43.4)	96 (47.5)	232 (41.9)	0.192
Duration, days	945.3 ± 1088.4	871.1 ± 1146.5	975.7 ± 1064.3	0.382
DPP4 inhibitor, n (%)	506 (66.9)	110 (54.5)	396 (71.5)	<0.001
Duration, days	945.1 ± 784.7	659.6 ± 717.0	1041.4 ± 784.0	<0.001
Insulin, n (%)	490 (64.8)	130 (64.4)	360 (65.0)	0.942
Immunosuppressant				
Steroid, n (%)	756 (100.0)	202 (100.0)	554 (100.0)	
Calcineurin inhibitors, n (%)	35 (97.2)	191 (94.6)	544 (98.2)	0.014
Tacrolimus, n (%)	646 (85.4)	175 (86.6)	471 (85.0)	0.659
Mean tacrolimus trough level, ng/mL	6.0 ± 1.5	6.4 ± 1.2	5.8 ± 1.5	<0.001
Cyclosporin, n (%)	138 (18.3)	20 (9.9)	118 (21.3)	<0.001

SGLT2i, sodium-glucose cotransporter 2 inhibitors; KT, kidney transplantation; DPP4, dipeptidyl peptidase 4.

Table S3. Serial comparisons of mean eGFR between the dipper and nondipper groups among SGLT2i users

Period (month)	Total (n = 211)	Dipper (n = 33)	Nondipper (n = 178)	t-statistics	*P*
0	69.5 ± 18.7	70.3 ± 15.8	69.4 ± 19.3	0.28	0.782
1	69.4 ± 17.7	67.1 ± 14.4	69.9 ± 18.2	−0.81	0.419
2	68.5 ± 17.8	65.9 ± 14.6	68.9 ± 18.3	−0.88	0.378
3	68.4 ± 17.7	67.2 ± 13.4	68.7 ± 18.4	−0.42	0.673
4	69.3 ± 17.8	67.1 ± 13.4	69.7 ± 18.5	−0.76	0.446
5	69.7 ± 17.9	69.2 ± 13.1	69.8 ± 18.7	−0.20	0.839
6	70.4 ± 18.0	69.1 ± 13.5	70.7 ± 18.7	−0.44	0.658
7	70.2 ± 18.0	69.1 ± 13.5	70.5 ± 18.7	−0.41	0.682
8	69.5 ± 18.1 (n = 130)	67.9 ± 13.9 (n = 24)	69.8 ± 19.0 (n = 106)	−0.92	0.358

eGFR, estimated glomerular filtration rate; SGLT2i, sodium-glucose cotransporter 2 inhibitor. *t-statistics and *P* value are a comparison of the nondipper and dipper groups at the same period.

Table S4. Multiple comparisons of mean eGFR changes from baseline in each dipper and nondipper group

Period (month)	Dipper (n = 33)	t-statistics	*P*	Nondipper (n = 178)	t-statistics	*P*
0	70.3 ± 15.8			69.4 ± 19.3		
1	67.1 ± 14.4	−2.54	0.011	69.9 ± 18.2	0.92	0.356
2	65.9 ± 14.6	−3.50	<0.001	68.9 ± 18.3	−0.84	0.402
3	67.2 ± 13.4	−2.47	0.014	68.7 ± 18.4	−1.33	0.183
4	67.1 ± 13.4	−2.59	0.010	69.7 ± 18.5	0.54	0.587
5	69.2 ± 13.1	−0.93	0.352	69.8 ± 18.7	0.86	0.389
6	69.1 ± 13.5	−0.94	0.350	70.7 ± 18.7	2.36	0.018
7	69.1 ± 13.5	−1.00	0.319	70.5 ± 18.7	2.01	0.045
8	67.9 ± 13.9 (n = 24)	−1.83	0.068	69.8 ± 19.0 (n = 106)	2.54	0.011

eGFR, estimated glomerular filtration rate.

*t-statistics and *P* value compare eGFRs between baseline and each period in the dipper and nondipper groups, respectively.

Table S5. Baseline characteristics between the dipper and nondipper groups

Variables	Total (n = 211)	Dipper (n = 33)	Nondipper (n = 178)	*P*
Age, y	51.5 ± 11.6	52.3 ± 14.1	51.3 ± 11.1	0.651
Sex, male, n (%)	149 (70.6)	19 (57.6)	130 (73.0)	0.114
Body mass index, kg/m^2	25.0 ± 3.6	24.8 ± 4.1	25.1 ± 3.5	0.665
Etiology of ESKD, DM, n (%)	127 (60.5)	21 (63.6)	106 (59.9)	0.833
Pretransplant RRT type, n (%)				0.308
Preemptive	51 (24.3)	6 (18.2)	45 (25.4)	
Hemodialysis	136 (64.8)	21 (63.6)	115 (65.0)	
Peritoneal dialysis	23 (11.0)	6 (18.2)	17 (9.6)	
Pretransplant dialysis vintage, y	2.1 ± 3.3	1.9 ± 3.0	2.2 ± 3.4	0.745
Pretransplant comorbidities, n (%)				
Diabetes mellitus	153 (72.5)	26 (78.8)	127 (71.3)	0.505
Hypertension	174 (82.5)	27 (81.8)	147 (82.6)	1.000
Ischemic heart disease	33 (15.6)	5 (15.2)	28 (15.7)	1.000
Cerebrovascular disease	23 (10.9)	4 (12.1)	19 (10.7)	1.000
Malignancy	12 (5.7)	2 (6.1)	10 (5.6)	1.000

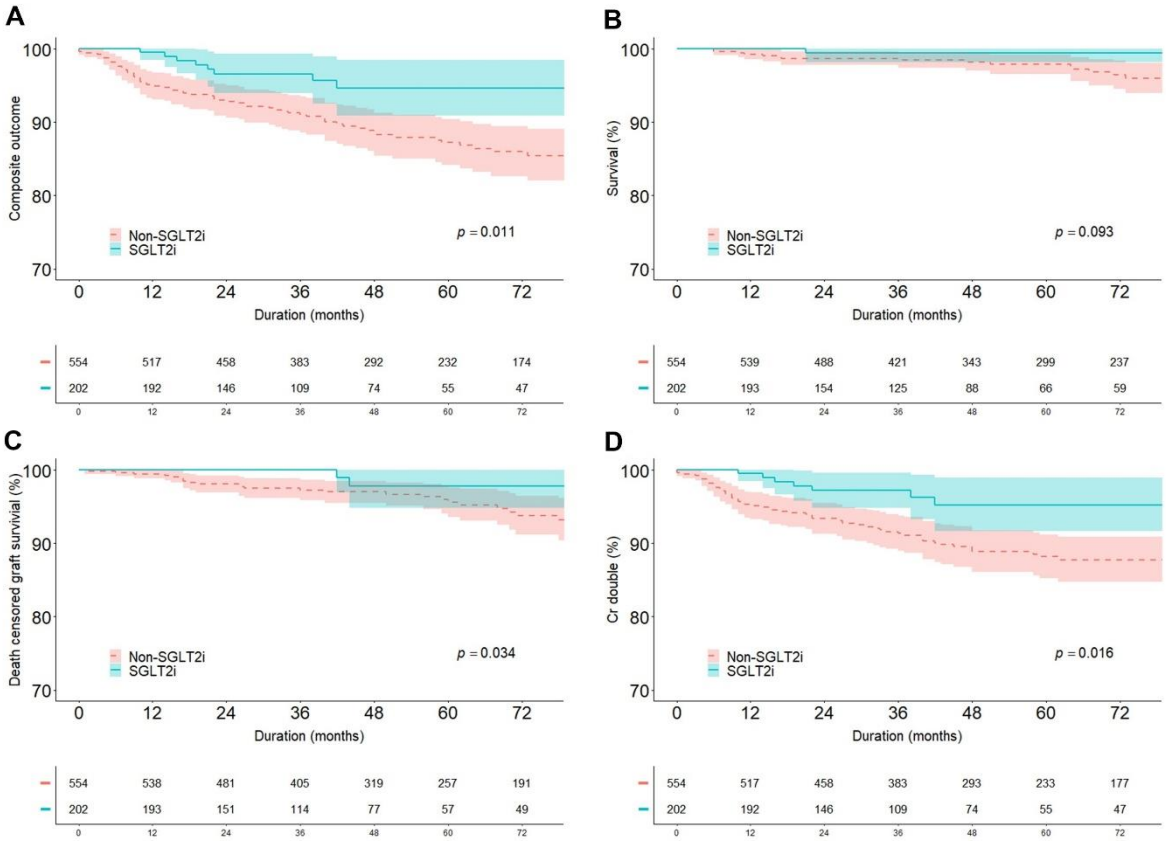
Chronic hepatitis B	8 (3.8)	0 (0.0)	8 (4.5)	0.456
Chronic hepatitis C	6 (2.8)	1 (3.0)	5 (2.8)	1.000
Donor age, y	46.5 ± 12.6	46.7 ± 11.3	46.5 ± 12.9	0.930
Donor sex, male, n (%)	92 (50.5)	16 (53.3)	76 (50.0)	0.893
Donor type, n (%)				0.951
Deceased	47 (22.3)	7 (21.2)	40 (22.5)	
Living-related	86 (40.8)	13 (39.4)	73 (41.0)	
Living-unrelated	78 (37.0)	13 (39.4)	65 (36.5)	
ABO incompatibility, n (%)	35 (16.6)	6 (18.2)	29 (16.3)	0.989
Laboratory findings at 3 months after KT				
Creatinine, mg/dL	1.2 ± 0.3	1.1 ± 0.2	1.3 ± 0.3	0.010
eGFR, mL/min/1.73 m^2	66.1 ± 17.0	66.2 ± 12.6	66.0 ± 17.7	0.941
Glucose, mg/dL	138.8 ± 60.9	135.4 ± 57.9	139.5 ± 61.7	0.728
HbA1c, %	7.3 ± 1.4	7.1 ± 1.2	7.4 ± 1.4	0.282
Laboratory findings at 12 months after KT				
Creatinine, mg/dL	1.2 ± 0.3	1.1 ± 0.2	1.2 ± 0.3	0.141
eGFR, mL/min/1.73 m^2	69.1 ± 17.1	67.2 ± 15.2	69.4 ± 17.4	0.549
Time from KT to SGLT2i	1403.5 ± 1652.3	632.4 ± 1536.5	1546.5 ± 1637.3	0.003

usage, days				
Antidiabetic medication after KT, n (%)				
Metformin	185 (87.7)	26 (78.8)	159 (89.3)	0.161
Sulfonylurea	97 (46.0)	11 (33.3)	86 (48.3)	0.163
DPP4 inhibitor	108 (51.2)	9 (27.3)	99 (55.6)	0.005
Insulin	129 (61.1)	14 (42.4)	115 (64.6)	0.027
Calcineurin inhibitors				
Tacrolimus, n (%)	178 (84.4)	26 (78.8)	152 (85.4)	0.485
Mean tacrolimus trough level, ng/mL	6.3 ± 1.3	7.2 ± 1.3	6.1 ± 1.3	<0.001
Cyclosporin, n (%)	25 (11.8)	2 (6.1)	23 (12.9)	0.408

ESKD, end-stage kidney disease; DM, diabetes mellitus; RRT, renal replacement therapy; KT, kidney transplantation; SGLT2i, sodium-glucose cotransporter 2 inhibitors; DPP4, dipeptidyl peptidase 4; eGFR, estimated glomerular filtration rate.

Table S6. The incidences of urinary tract infection

Type of UTI	SGLT2i users		SGLT2i nonusers		RR	95% CI
	n	Events/100 patient-year	n	Events/100 patient-year		
Any	12	4.5	661	6.2	0.74	0.42–1.31
Bacteria	11	4.2	652	6.1	0.69	0.38–1.25
Fungus	1	0.4	31	0.2	1.31	0.18–9.61

UTI, urinary tract infection; SGLT2i, sodium-glucose cotransporter 2 inhibitors; RR, relative risk; CI, confidence interval.

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