Effects and Mechanisms of Dapagliflozin Treatment on Ambulatory Blood Pressure in Diabetic Patients with Hypertension

Authors' Contribution:
Study Design **A**
Data Collection **B**
Statistical Analysis **C**
Data Interpretation **D**
Manuscript Preparation **E**
Literature Search **F**
Funds Collection **G**

BCDE 1 **Zirui Hao**
BF 1 **Yue Sun**
BF 1 **Yingzhen Wen**
BF 1 **Lijuan Cui**
DF 1 **Guiping Li**
AG 2 **Yan Liu**

1 Department of Endocrinology, The Third People's Hospital of Huizhou, Huizhou, Guangdong, P.R. China
2 Department of Cardiology, The Third People's Hospital of Huizhou, Huizhou, Guangdong, P.R. China

Corresponding Author: Yan Liu, e-mail: doctorliuyan168@sina.com
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Background: Studies have shown that dapagliflozin has antihypertensive effects. However, the effects and mechanisms of dapagliflozin on ambulatory blood pressure (ABP) have not been fully evaluated. In this study, we aimed to evaluate the effects of dapagliflozin treatment on ABP in patients with type 2 diabetes and hypertension.

Material/Methods: Patients were prospectively enrolled and divided into 2 groups: dapagliflozin treatment group (n=182) and no dapagliflozin treatment group (n=304). Clinical characteristics and measures of treatment, serum uric acid (SUA), 24-h urinary UA (UUA) excretion, and 24-h ABP were collected. The effects and mechanisms of dapagliflozin on 24-h ABP were evaluated.

Results: After 3 months, the patients without dapagliflozin treatment had higher SUA, lower 24-h UUA excretion, and higher 24-h and daytime systolic blood pressure (SBP) (P<0.05) compared to patients with dapagliflozin treatment. After adjusting for covariates, results showed that dapagliflozin treatment was significantly associated with reduced 24-h SBP (β=–0.29 and P=0.02) and reduced daytime SBP (β=–0.33 and P=0.009). After additionally adjusting for SUA and 24-h UUA excretion, there were no significant relationships found between dapagliflozin treatment and 24-h (β=–012, P=0.10) and daytime SBP (β=–0.20, P=0.06).

Conclusions: In patients with diabetes and hypertension, dapagliflozin treatment was associated with reduced 24-h and daytime SBP, which could be related to the drug's effect of increasing 24-h UUA excretion.

MeSH Keywords: **Arterial Pressure • Diabetes Complications • Uric Acid**

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Background

Diabetes mellitus is a major risk factor for cardiovascular and renal diseases [1,2]. In the past decade, several novel antidiabetic medications have been developed, and among these, sodium-glucose cotransporter-2 inhibitors (SGLT2i) have consistently shown promising cardio- and renoprotective effects [3–7]. For example, the DAPA-HF (Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction) trial showed that dapagliflozin therapy is beneficial in reducing cardiovascular and all-cause mortality in diabetic and nondiabetic patients with heart failure [4]. In patients with diabetes and chronic kidney disease, canagliflozin significantly reduces major adverse cardiovascular events and kidney failure [6]. In patients with diabetes who have increased cardiovascular risk, empagliflozin therapy is associated with better renal function and a lower risk of renal events compared to that of placebo [7]. Unfortunately, most participants in these major clinical trials were white, and the cardiovascular and renal benefits of SGLT2i in a Chinese patient population with diabetes have not been as thoroughly investigated. Recognizing the increasing prevalence and incidence of diabetes mellitus in Chinese populations [8,9] and the racial and ethnic differences in the clinical characteristics and prognosis of diabetes mellitus, it is imperative to carefully evaluate the safety and efficacy of SGLT2i in Chinese diabetic populations.

Hypertension is a common comorbidity in patients with diabetes [10]. Numerous studies have shown that the presence of hypertension was associated with a higher cardiovascular and renal risk in diabetic patients than in their counterparts without hypertension [11–13]. Importantly, some studies have reported that in addition to lowering blood glucose levels, SGLT2i lower blood pressure (BP), which might be due to their natriuretic and diuretic effects [14,15]. However, whether these benefits also exist in the Chinese population are unknown. In addition, the effects and mechanisms of SGLT2i on 24-h ambulatory blood pressure (ABP) have not been fully investigated.

Herein, leveraging data from our ongoing prospective diabetic and hypertensive cohort study, we evaluated the effects of 3 months of dapagliflozin treatment on 24-h ABP in patients with diabetes and hypertension. In addition, because few studies have reported that SGLT2i increase urinary uric acid (UUA) excretion [16,17], we evaluated whether a change in 24-h ABP was mediated by an increase in UUA excretion and the resultant reduction in serum UA (SUA) with dapagliflozin treatment.

Material and Methods

Study participants

This study was approved by the Institutional Review Board of the Third People's Hospital of Huizhou (approval no. TPHHZ-20180627301), and written inform consent was obtained before participants' enrollment. The inclusion criteria were as follows: >18 years old; type 2 diabetes mellitus; primary hypertension; 24-h ABP measurement at baseline and 3 months after dapagliflozin treatment; and baseline estimated glomerular filtration rate (eGFR) ≥60 mL/min/1.73 m^2. The exclusion criteria were as follows: prior history of diabetic ketone acidosis or hyperosmolar coma; documented secondary hypertension; treatment with UA-lowering medications; treatment with a diuretic at baseline or follow-up; any cardiovascular or renal event from baseline to the 3-month follow-up; missing 24-h urine collection, SUA, or blood glucose measurements.

Data collection

A structured questionnaire was used for prospective data collection by 2 independent investigators. Baseline data included demographics (age and sex), anthropometrics (office BP, heart rate, weight, height, and risk factors and comorbidities (obesity, cigarette smoking, hyperuricemia, dyslipidemia, atrial fibrillation, congestive heart failure, coronary heart disease, ischemic stroke/transient ischemic attack, peripheral arterial disease, and obstructive sleep apnea). At baseline and the 3-month follow-up, fasting venous plasma was drawn to evaluate fasting plasma glucose, glycated hemoglobin (HbA1c), total cholesterol, triglycerides, SUA, serum creatinine, and C-reactive protein levels; a 24-h urinary specimen was collected for the analysis of 24-h urine volume, UUA, and urinary creatinine and albumin excretion. The 24-h UAA was indexed to body surface area, and the urinary albumin to creatinine ratio (UACR) was calculated as urinary albumin/urinary creatinine. Body mass index (BMI) was calculated by weight in kg divided by height in squared meters, and BMI ≥28 kg/m^2 was defined as obesity based on the WHO recommendation for Asian populations [18]. Hyperuricemia was defined as SUA ≥420 umol/L in men and ≥360 umol/L in women. Creatinine was used to calculate eGFR based on the Modification of Diet in Renal Disease formula as previously described [19]. The 24-h ABP measurements were performed based on a prior description [20], whereby ABP was recorded from the non-dominant arm for 24 h at 20-min intervals during the day (06:00–22:00) and at 30-min intervals during the night (22:00–06:00) using a portable BP monitoring device (model 90207, Space-Labs Medical Inc, Redmond, WA, USA). The medications used were at physicians' discretion and were collected from the electronic health records. All data were entered into encrypted Excel datasets.
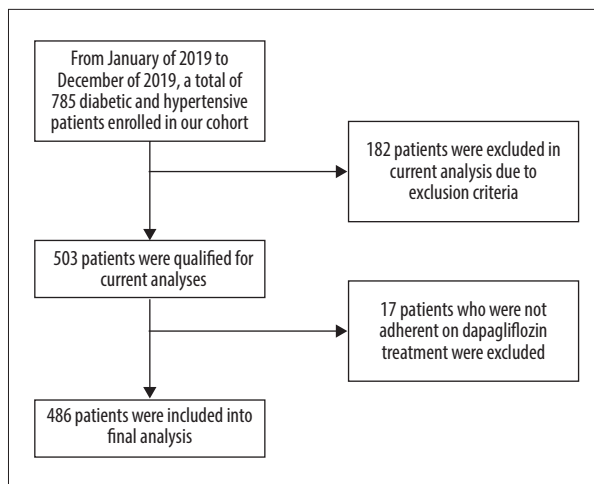
From January of 2019 to December of 2019, a total of 785 diabetic and hypertensive patients enrolled in our cohort

182 patients were excluded in current analysis due to exclusion criteria

503 patients were qualified for current analyses

17 patients who were not adherent on dapagliflozin treatment were excluded

486 patients were included into final analysis

Figure 1. Study flowchart.

Statistical analysis

Study participants were divided into 2 groups: with and without dapagliflozin treatment. Continuous variables were presented as mean±standard deviation (SD) or median (interquartile range), and between-group differences were evaluated using a *t* test or Mann-Whitney-Wilcoxon test, as appropriate. Categorical variables were presented as number and proportion (%), and between-group differences were evaluated using a chi-squared test or Fisher exact test, as appropriate. Linear regression analysis was performed to evaluate the relationship between 24-h ABP and dapagliflozin treatment. All analyses were performed using SPSS version 23.0 and a 2-sided *P*-value of <0.05 was considered statistically significance.

Results

Comparison of baseline characteristics

From January 2019 to December 2019, a total of 486 participants were enrolled in our study (Figure 1). Participants were separated into 2 groups: with dapagliflozin treatment and without dapagliflozin treatment. In brief, patients in the dapagliflozin treatment group received a dose of 5 mg of dapagliflozin per day. Comparisons of baseline characteristics are presented in Table 1. Compared to patients with dapagliflozin treatment, patients without dapagliflozin treatment were younger, had a higher BMI and triglyceride levels, and were more likely to be female and obese (*P*<0.05).

Comparisons of UA and ABP at baseline and 3-month follow-up

As presented in Table 2, there were no significant differences in SUA, 24-h UUA, UACR, and 24-h ABP at baseline between the 2 groups. At the 3-month follow-up, compared to patients with dapagliflozin treatment, patients without dapagliflozin treatment had higher SUA and UACR, and a lower 24-h urine volume and UUA excretion (*P*<0.05). In addition, the 24-h and daytime systolic BP (SBP) were higher in patients without dapagliflozin than in patients with dapagliflozin treatment (*P*<0.05).

Comparisons of medications used at baseline and 3-month follow-up

The lists of medications used at baseline and at the 3-month follow-up are shown in Table 3. At baseline, the use of angiotensin-converting enzyme inhibitor/angiotensin receptor blockers (ACEI/ARB) was higher and the use of calcium channel blockers (CCB) was lower in patients without dapagliflozin treatment than in patients with dapagliflozin treatment (*P*<0.05). The use of antidiabetic drugs at baseline was similar in both groups. At the 3-month follow-up, the use of beta-blockers and CCB was decreased in the dapagliflozin group, and the use of ACEI/ARB and CCB was increased in patients without dapagliflozin treatment. The between-group difference in ACEI/ARB use remained the same from baseline to follow-up. In addition, the use of metformin, sulfonylureas, and alpha-glucoside inhibitors increased in patients without dapagliflozin treatment, and was higher than in patients with dapagliflozin treatment. Compared to baseline, the use of metformin, sulfonylureas, alpha-glucoside inhibitors and other antidiabetic medications decreased at the 3-month follow-up in patients with dapagliflozin treatment. In both groups, fasting plasma glucose and HbA1c levels were reduced similarly at the 3-month follow-up compared to the levels at baseline. No adverse effects including hypoglycemia, hypotension, hyponatremia, and acute kidney injury were reported in either group.

Relationship between 24-h ABP and dapagliflozin treatment

As presented in Table 4, before adjusting for covariates, dapagliflozin treatment was associated with a lower 24-h SBP, daytime SBP, and nighttime SBP, and there was no significant relationship between dapagliflozin treatment and ambulatory diastolic BP. After adjustment for potential covariates, dapagliflozin treatment remained significantly associated with 24-h SBP ($\beta=-0.29$, $R^2=0.25$, and *P*=0.02) and daytime SBP ($\beta=-0.33$, $R^2=0.32$, and P-value=0.009). However, after further adjusting for SUA and 24-h UUA excretion at follow-up, there were no significant associations between dapagliflozin treatment and 24-h SBP ($\beta=-012$, $R^2=0.14$, and *P*=0.10) and daytime SBP ($\beta=-0.20$, $R^2=0.1$, and *P*=0.06).

Table 1. Comparison of patient baseline characteristics.

Variables	With dapagliflozin (n=182)	Without dapagliflozin (n=304)	P
Age (years)	43.7±13.3	41.1±14.6	0.03
Female, n (%)	55 (30.2)	108 (35.5)	0.01
Duration of diabetes (years)	3.6 (1.4–8.9)	3.4 (1.2–8.2)	0.14
Duration of hypertension (years)	6.8 (3.3–10.4)	6.6 (3.1–9.9)	0.71
Office SBP (mmHg)	143±20	144±21	0.82
Office DBP (mmHg)	86±17	85±16	0.77
Heart rate (beat per min)	74±16	75±17	0.53
Body mass index (kg/m²)	24.2±6.3	24.9±6.5	0.008
Obesity, n (%)	58 (31.9)	105 (34.6)	0.02
Smoking, n (%)	70 (38.5)	118 (38.8)	0.26
Hyperuricemia, n (%)	63 (34.6)	107 (35.2)	0.32
Dyslipidemia, n (%)	78 (42.9)	128 (42.1)	0.95
Atrial fibrillation, n (%)	12 (6.6)	25 (8.2)	0.09
Congestive heart failure, n (%)	20 (10.9)	31 (10.2)	0.10
Coronary heart disease, n (%)	38 (20.9)	66 (21.7)	0.22
Ischemic stroke/TIA, n (%)	18 (9.9)	31 (10.2)	0.31
Peripheral arterial disease, n (%)	10 (5.5)	19 (6.3)	0.41
Obstructive sleep apnea, n (%)	23 (12.6)	34 (11.2)	0.61
Total cholesterol (mmol/L)	5.1±0.9	5.2±1.0	0.18
Triglyceride (mmol/L)	1.7 (0.8–2.6)	1.9 (0.9–2.7)	0.04
Creatinine (umol/L)	70.4±15.3	69.2±15.5	0.51
eGFR (ml/min/1.73m2)	80.8±15.4	79.6±14.8	0.22
C-reactive protein (mg/dL)	3.0±1.1	3.2±1.0	0.13

SBP – systolic blood pressure; DBP – diastolic blood pressure; TIA – transient ischemic attack; eGFR – estimated glomerular filtration rate; * $P<0.05$.

Discussion

The present study has 3 main findings. First, dapagliflozin treatment increased 24-h UUA secretion; second, dapagliflozin treatment was associated with a reduced 24-h SBP and daytime SBP after 3 months of treatment; and third, the BP-lowering benefits of dapagliflozin treatment were at least partly attributable to its increasing 24-h UUA excretion. To the best of our knowledge, this is the first study to evaluate the effects of dapagliflozin on 24-h ABP in Chinese patients with diabetes and hypertension. This study's findings provide novel insights into the effects and mechanisms of dapagliflozin on 24-h ABP reduction. Further studies with larger sample sizes

and longer follow-up periods are needed to evaluate whether these findings can benefit diabetic patients with hypertension.

Hypertension is prevalent in patients with diabetes [21–23]. Kabakov et al. reported that among patients with type 2 diabetes, the prevalence of hypertension is 60.2% [22]; and a systematic review reported this prevalence is as high as 75% [23]. Notably, the presence of hypertension is associated with poor prognosis in patients with diabetes [10]. Dapagliflozin is a novel antidiabetic medication. Through inhibiting SGLT2 in the renal proximal tubule, dapagliflozin increases urinary glucose excretion. In addition, experimental and human studies have shown that dapagliflozin could increase urinary sodium excretion and result in diuresis and

Table 2. Uric acid and ambulatory blood pressure at baseline and 3-month follow-up.

Variables	With dapagliflozin (n=182)	Without dapagliflozin (n=304)	P
At baseline			
Serum uric acid (umol/L)	416±53	410±47	0.16
24-h urine volume (mL)	1780±236	1733±209	0.33
24-h urinary uric acid (mmol/24 h/1.73 m^2)	2.6±0.4	2.5±0.4	0.62
UACR (mg/mmol)	43.6 (18.9–238.3)	45.2 (20.1–260.1)	0.09
24-h SBP (mmHg)	132±13	133±14	0.41
24-h DBP (mmHg)	79±12	78±13	0.51
Daytime SBP (mmHg)	137±16	137±17	0.96
Daytime DBP (mmHg)	83±15	84±14	0.75
Nighttime SBP (mmHg)	123±12	122±13	0.66
Nighttime DBP (mmHg)	74±13	73±12	0.38
At 3-month follow-up			
Serum uric acid (umol/L)	387±40	404±42	0.006
24-h urine volume (mL)	1838±207	1669±194	<0.001
24-h urinary uric acid (mmol/24 h/1.73 m^2)	2.9±0.7	2.4±0.3	0.01
UACR (mg/mmol)	40.8 (16.5–207.6)	45.6 (20.7–262.5)	0.009
24-h SBP (mmHg)	129±11	133±15	0.03
24-h DBP (mmHg)	78±10	79±11	0.24
Daytime SBP (mmHg)	132±13	137±16	0.02
Daytime DBP (mmHg)	81±12	83±13	0.35
Nighttime SBP (mmHg)	121±11	122±11	0.19
Nighttime DBP (mmHg)	72±10	73±11	0.38

UACR – urine albumin-creatinine ratio; SBP – systolic blood pressure; DBP – diastolic blood pressure; * $P<0.05$

natriuresis. Compared to placebo, SGLT2i were associated with a significant reduction of office BP. Some studies have also reported that among patients with type 2 diabetes, empagliflozin, taken with antihypertensive medications, significantly reduces 24-h, daytime, and nighttime SBP [24]. Additionally, a meta-analysis showed that SGLT2i significantly reduce 24-h ambulatory systolic and diastolic BP by 3.76 mmHg and 1.83 mmHg, respectively [25]. Consistent with the previous research, the present study demonstrated that mean 24-h and daytime SBP were reduced by 4 mmHg and 5 mmHg, respectively, after 3 months of dapagliflozin treatment. Notably, the use of antihypertensive medications (beta-blockers and CCB) was reduced in the dapagliflozin treatment group, suggesting that the observed 24-h SBP and daytime SBP reductions were attributable to dapagliflozin treatment rather than to an increased use of antihypertensive medications.

Uric acid has been considered an independent risk factor for hypertension development and BP progression. For example,

Perlstein et al. reported that SUA independently predicted hypertension development after adjustment for risk factors [26]. Also, Krupp et al. reported that patients with hyperuricemia were at an increased risk of hypertension, regardless of age [27]. Despite convincing evidence demonstrating that increased SUA was associated with BP elevation and hypertension development, no randomized clinical trials have been conducted to determine if lowering SUA can decrease BP. The present findings suggest that 3 months of dapagliflozin treatment significantly reduced SUA through increasing 24-h UUA excretion, which was consistent with previous reports [16,17]. Based on our present linear regression analysis, we postulate that the effects of SGLT2i on BP reduction are more likely due to SUA reduction and less likely due to 24-h urine volume change. Indeed, after adjusting for 24-h urine volume, dapagliflozin treatment remained significantly associated with 24-h and daytime SBP. However, after making further adjustments for SUA and 24-h UUA excretion, dapagliflozin treatment was no

Table 3. Medications use at admission and 3-month follow-up.

Variables	With dapagliflozin (n=182)		Without dapagliflozin (n=304)		P
At admission					
Aspirin, n (%)	65	(35.7)	115	(37.8)	0.11
Statins, n (%)	73	(40.1)	123	(40.5)	0.821
ACEI/ARB, n (%)	80	(44.0)	162	(53.3)	0.007
Beta-blocker, n (%)	34	(18.7)	52	(17.1)	0.261
Calcium channel blocker, n (%)	59	(32.4)	66	(21.7)	0.02
No. antihypertensive drugs	1.6	(0.8–2.4)	1.5	(0.7–2.3)	0.31
Metformin, n (%)	158	(85.9)	262	(86.2)	0.19
Sulfonylureas, n (%)	80	(43.5)	131	(43.1)	0.99
Alpha-glucoside inhibitor, n (%)	38	(20.9)	63	(20.7)	0.91
GLP-1 agonist, n (%)	16	(8.8)	29	(9.6)	0.76
DDP-4 inhibitor, n (%)	13	(7.1)	24	(7.9)	0.45
Thiazolidinedione, n (%)	0		2	(0.7)	–
Insulin, n (%)	15	(8.2)	27	(8.9)	0.22
No. antidiabetic drugs	1.7	(0.8–2.6)	1.8	(0.9–2.8)	0.17
Fasting plasma glucose (mmol/L)	6.3±0.5		6.2±0.4		0.60
HbA1c (%)	7.1±1.0		7.0±0.9		0.33
At 3-month follow-up					
Aspirin, n (%)	65	(35.7)	115	(37.8)	0.10
Statins, n (%)	73	(40.1)	123	(40.5)	0.82
ACEI/ARB, n (%)	80	(44.0)	168	(55.3)	0.002
Beta-blocker, n (%)	31	(17.0)	52	(17.1)	0.19
Calcium channel blocker, n (%)	50	(27.2)	77	(25.3)	0.37
No. antihypertensive drugs	1.5	(0.7–2.3)	1.6	(0.8–2.5)	0.25
Metformin, n (%)	128	(69.6)	282	(92.8)	<0.001
Sulfonylureas, n (%)	35	(19.0)	140	(46.1)	0.01
Alpha-glucoside inhibitor, n (%)	16	(8.7)	69	(22.7)	0.04
GLP-1 agonist, n (%)	10	(5.4)	36	(11.8)	0.09
DDP-4 inhibitor, n (%)	6	(3.3)	32	(10.5)	0.12
Thiazolidinedione, n (%)	0		4	(1.3)	–
Insulin, n (%)	8	(4.3)	32	(10.5)	0.20
Dapagliflozin, n (%)	182	(100)	0		–
No. antidiabetic drugs	2.1	(1.0–2.8)	2.0	(0.9–2.7)	0.15
Fasting plasma glucose (mmol/L)	6.0±0.4		6.1±0.3		0.32
HbA1c (%)	6.9±0.8		6.9±0.7		0.93

ACEI/ARB – angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; GLP-1 agonist – glucagon-like peptide-1 agonist; DDP-4 inhibitor – dipeptidyl peptidase-4 inhibitor; HbA1c – glycated hemoglobin A1c; * P<0.05.

Table 4. Relationship between 24-h ABP and dapagliflozin treatment.

	β	R²	P
24-h SBP			
Unadjusted	−0.58	0.37	<0.001
Adjusted model 1	−0.29	0.25	0.02
Adjusted model 2	−0.12	0.14	0.10
24-h DBP			
Unadjusted	−0.14	0.10	0.18
Adjusted model 1	−0.06	0.05	0.34
Adjusted model 2	−0.02	0.02	0.63
Daytime SBP			
Unadjusted	−0.62	0.41	<0.001
Adjusted model 1	−0.33	0.32	0.009
Adjusted model 2	−0.20	0.19	0.06
Daytime DBP			
Unadjusted	−0.16	0.11	0.12
Adjusted model 1	−0.09	0.05	0.23
Adjusted model 2	−0.03	0.02	0.40
Nighttime SBP			
Unadjusted	−0.30	0.26	0.04
Adjusted model 1	−0.11	0.12	0.09
Adjusted model 2	−0.07	0.08	0.21
Nighttime DBP			
Unadjusted	−0.10	0.14	0.32
Adjusted model 1	−0.07	0.06	0.48
Adjusted model 2	−0.03	0.02	0.63

SBP – systolic blood pressure; DBP – diastolic blood pressure. Model 1: adjusted for age, female sex, body mass index, estimated glomerular filtration rate, medication use at follow-up (aspirin, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker, calcium channel blocker, beta-blocker, and metformin); and glycated hemoglobin A1c, urine albumin-creatinine ratio and 24-h urine volume at follow-up. Model 2: was additionally adjusted for serum uric acid and 24-h urinary uric acid excretion at follow-up.

longer significantly associated with 24-h and daytime SBP. In addition, several potential mechanisms of the antihypertensive effects of SGLT2i have been postulated. For example, SGLT2 is co-expressed with the Na+/H+ exchanger-3 membrane protein in the early proximal renal tubule. SGLT2 inhibition with dapagliflozin can enhance natriuresis, which can in turn increase sodium excretion and lower BP [28]. Furthermore, via osmotic diuresis induced by urinary glucose and sodium excretion, SGLT2i reduced BP in diabetic patients [15]. Weight loss associated with SGLT2i treatment can also contribute to BP reduction, as was shown in a pooled analysis of 2 randomized placebo-control trials [29]. Moreover, SGLT2i have been shown to improve arterial stiffness [30] and suppress the renal renin-angiotensin system [31], which together might reduce BP.

It is worth mentioning that, as shown in Table 1, several factors associated with BP, including age, sex, BMI, and obesity, were significantly different between the dapagliflozin treatment and no dapagliflozin treatment groups. One can speculate that these differences contribute to the observed between-group differences in 24-h and daytime SBP. Nonetheless, after adjustment for the potential confounding factors (Table 4), dapagliflozin treatment was still significantly associated with reduced 24-h and daytime SBP, further supporting the benefits of dapagliflozin for BP reduction. Interestingly, some studies have shown that aspirin treatment can reduce BP because of its anti-inflammatory effects [32], while other studies did not show any antihypertensive effects of aspirin treatment [33]. In the present study, the use of aspirin in the 2 groups was comparable at baseline and 3-month follow-up. The inclusion

of aspirin use in the linear regression model (Table 4) did not influence the relationship between dapagliflozin and 24-h or daytime ABP, suggesting that aspirin did not have a major effect on BP change in the current study.

This study has some limitations. First, this is an observational study and findings from the analysis cannot be used to make conclusions about causal relationships. Second, this study was conducted in a Chinese population, and it is not known whether these findings can be extrapolated to other racial and ethnic groups. Third, this was a short-term study and further studies are needed to evaluate the long-term safety and efficacy of dapagliflozin treatment in this population. Fourth, it is important to also evaluate whether BP-lowering dapagliflozin treatment can reduce cardiovascular events. Lastly, although we have adjusted for potential covariates, undetected and unknown biases might have influenced the results that indicated the relationship between dapagliflozin treatment and 24-h and daytime SBP.

Conclusions

In conclusion, our results showed that dapagliflozin treatment was associated with 24-h and daytime SBP reduction in patients with diabetes and hypertension, and this benefit might be due to its effect on increasing 24-h UUA excretion.

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Conflict of interest

None.

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