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Factors associated with a higher need for antihypertensive medications at 12-months in postkidney transplant recipients: a retrospective cohort study

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Background: There are limited data on why some kidney transplant (KTx) recipients (KTRs) have 'difficult-to-control (DTC) hypertension' requiring greater than or equal to 2 antihypertensive medications while others require less antihypertensive medications post-KTx.

Methods: The authors reviewed the pre-KTx cardiovascular (CV) imaging, and the changes of CV risk factors during the first-year post-KTx. The authors divided patients according to the number of their blood pressure medications at one year into two groups: requiring less than or equal to 1 and requiring greater than or equal to 2 medications (DTC hypertension). The target blood pressure during the time of this study was less than 140/90 mmHg.

Results: Two hundred forty-five KTRs were included with an average age of 43.2. 56.3% were male and 79.2% were living donor KTRs. Pre-emptive KTx was 6.5%, previous coronary artery disease was 12.7%, diabetes and smoking 40.8 and 9%, respectively. 38% of the patients had DTC HTN. Risk factors were age ($P < 0.01$), pre-KTx hypertension ($P < 0.01$), and diabetes mellitus ($P < 0.01$). Dialysis vintage, type of dialysis, type of KTx, and smoking were not different between the groups. Patients with abnormal pre-KTx CV imaging, including abnormal ejection fraction less than 55% ($P = 0.03$), abnormal wall motion on echocardiography ($P < 0.01$), abnormal perfusion stress test ($P < 0.01$), higher calcium scoring ($P < 0.01$), abnormal cardiac catheterization ($P < 0.01$), or higher degree of calcifications on CT of pelvic arteries ($P < 0.01$) were at higher risk of DTC hypertension. Post-KTx factors including rejection, change in serum creatinine and weight, A1c, new-onset diabetes post-KTx, and persistent hyperparathyroidism were not different between the groups. Multivariate analysis revealed associations with age (aOR = 1.027), male sex (aOR = 2.057), baseline diabetes mellitus (aOR = 2.065), baseline HTN (aOR = 2.82), and use of greater than or equal to 2 antihypertensive medications at 1-month post-KTx (aOR = 6.146).

Conclusion: At one year post transplantation, about a third of the KTRs required had DTC HTN. These patients were more likely to be older, males, diabetics, previously hypertensive, on greater than or equal to 2 HTN medications at 1-month post-KTx, and to have abnormal baseline pretransplant CV imaging.

Keywords: antihypertensive drugs, arterial hypertension, blood pressure, hypertension, kidney transplant recipients, kidney, transplantation

Introduction

Kidney transplantation (KTx) significantly decreases cardiovascular (CV) risk among KTx recipients (KTRs) compared to dialysis[1], but their CV risk remains much higher than general population[1], and CV disease remains the leading cause of mortality[2]. Hypertension (HTN), new-onset diabetes after transplant, weight gain, dyslipidemia, and immunosuppression are among several factors that contribute to this increased CV risk post-KTx. Post-KTx HTN, which is defined as a persistently elevated blood pressure (BP) or normotension with the use of antihypertensive medications after successful KTx[3], is very

HIGHLIGHTS

- In our center, approximately one-third of kidney transplant recipients required two or more blood pressure medications one year post-transplant.
- Patients who required two or more blood pressure medications were more likely to be older, male, diabetics, previously hypertensive, and have abnormal pretransplant cardiovascular imaging.
- Post-transplant factors such as rejection, change in serum creatinine, and weight were not significantly different between the two groups.

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common (up to 90% of KTRs)[4]. Uncontrolled HTN post-KTx is associated not only with decreased graft survival but also with CV disease and mortality post-KT[3,5,6].

The pathophysiology behind post-KTx HTN is multifactorial[4]. Pre-existing pre-KTx vascular pathologies due to established HTN and chronic kidney disease contribute to elevated BP and increased pulse pressure in KTRs[7]. After KTx, multiple factors can also lead to or exacerbate post-KTx HTN. These factors include immunosuppressant therapy like calcineurin inhibitors and glucocorticoids[8–10], altered sodium regulation and the activation of the renin–angiotensin–aldosterone system (RAAS)[11], obesity and post-KTx weight gain[12], transplant renal artery stenosis[13], volume overload, and allograft insufficiency[14]. In addition, donor factors such as poor allograft quality, increased age, pre-existing HTN, and genetic factors can also contribute to the development of post-KTx HTN[3].

Early after KTx, BP is influenced by volume expansion and the high doses of steroids and calcineurin inhibitors used at transplantation. With time, graft function and volume status improve, and BP become more stable[15]. In general, KTRs tend to require less antihypertensive medications than prior to transplantation. Kubo *et al.*[16] showed that the mean number of antihypertensive medications dropped from 3.3 ± 1.6 to 2.1 ± 0.9 post-KTx. Similarly, Midtvedt *et al.*[17] showed that KTRs after bilateral nephrectomy, require less the antihypertensive agents' requirements from a mean of 2.3 ± 0.5 drugs/day pre-KTx to 1.3 ± 0.9 drugs/day post-KTx. However, some KTRs continue to require several antihypertensive medications to achieve adequate control 'difficult-to-control (DTC) HTN'. In a study by Małyszko *et al.*[18] on 150 KTRs, 60% required three or more antihypertensive agents, with only 40% demonstrating target BP levels of <130/80 mmHg. Similarly, Kaul *et al.*[19] showed that almost 52% of the KTx patients required three or more antihypertensive agents at 6 months post-KTx. Differential diagnosis of DTC HTN includes reduced compliance, white coat HTN, or true resistant HTN, which requires the use of three types of antihypertensive medications including a diuretic at maximum tolerated doses[20–22].

To date, there has not been a clear BP treatment objective for KTRs, due to a lack of sufficient randomized controlled trials to establish the advantages of reducing BP levels on graft and patient, and no specific antihypertensive agent has been shown to improve patient or graft survival over others[3,23,24]. Additionally, it is still not clear if the higher need of antihypertensive medications is related to demographic factors, cardiac factors, or post-KTx changes. More specifically, studies assessing post-KTx HTN and its associated factors in an Arab population are limited and outdated. The present study was conducted to identify risk factors leading to a higher need of antihypertensive agents, to aid in understanding, anticipating, and treating DTC HTN post-KTx. We examined the risk factors for patients requiring greater than or equal to 2 anti-HTN medications at 1-year post-KTx.

Methodology

Study design

The pre-KTx CV risk assessment at our center is performed according to the AHA/ACC 2013 guidelines[25,26]. Echocardiography is requested for all KTx candidates. A positron emission tomography stress test is performed in those who have greater than or equal to 3 CV risk factors, limited functional status or abnormal echo findings. The decision of cardiac catheterization is deferred to the cardiologists' assessment. A computed tomography (CT) scan with contrast is done to assess the extent of the vascular calcification/ atherosclerosis of the abdomen and pelvis. This test is performed in most of the KTx patients, unless they are at low surgical risk or they are at higher risk of losing their residual renal function (e.g. on peritoneal dialysis or undergoing pre-emptive transplantation)[25].

After KTx, KTRs are followed closely during the first-year post-KTx. The maintenance immunosuppression protocol consists of tacrolimus, mycophenolate, and prednisolone[27]. BP is monitored at each clinic visit and antihypertensive medications are adjusted as clinically indicated. The target BP was less than 140/90 mmHg as per the relevant guidelines during the study's period[28]. Calcium channel blockers (nifedipine or amlodipine) are typically used as a first-line antihypertensive treatment post-KTx, followed by a β-blocker. Hydralazine, clonidine, α-blockers, and angiotensin-converting enzyme inhibitors are used, respectively, as add-on therapies[27].

We divided patients according to the number of BP medications at one year into two groups; those who required less than or equal to 1 anti-HTN medications, and those who required greater than or equal to 2 medications, defined as the DTC group.

Data collection

After the approval by the local institutional review board, a retrospective study was conducted at a large tertiary medical center. The informed consent was waived by the institutional review board due to the retrospective nature of this study. Patients 18 years or older who underwent KTx between 1 January 2017, and 30 May 2020, and were followed up for at least 12 months at our center were included in this study. This manuscript has been reported according to the Strengthening the Reporting of Cohort Studies in Surgery (STROCSS) 2019 guidelines[29].

Clinical information was obtained from electronic medical records including patients' demographics, baseline CV risk factors, pre-KTx cardiac imaging and the changes of different variables during the 1-year post-KTx. Pre-KTx cardiac imaging included the findings of echocardiography, positron emission tomography stress test, coronary angiogram, and abdomen and pelvis vascular CT scan with contrast. Additionally, systolic (SBP) and diastolic BP (DBP) at baseline (pre-KTx), 1-, 6-, and 12 months post-KTx, and the number of antihypertensive medications, at 1- and 12-post-KTx months were analyzed.

Statistical Analysis

We used SPSS 26 (IBM, Armonk) for the analysis. Continuous variables are presented as mean ± SD. The Shapiro–Wilk test was used to assess the normality of continuous variables and guide the selection of a parametric or nonparametric test for the comparison of variables. The variables were compared using Welch's *t*-test, Student *t*-test, and the Mann–Whitney-*U* test. Categorical variables are presented as frequencies and percentages and compared using the χ^2 or Fisher's exact tests, as appropriate. To adjust for confounding factors, clinically relevant variables were included in the multivariate logistic regression model to examine the association between patient characteristics and the need for more

Table 1

Baseline patients' characteristics

	Total $n=245$ (%)	≤1 HTN medication $n=151$ (%)	≥2 HTN medications $n=94$ (%)	P
Demographics and baseline CV risk factors				
Age (years)*	43.2 ± 16	38.6 ± 14.8	50.6 ± 15.1	< 0.001
Sex				
Female	107 (43.7)	79 (52.3)	28 (29.8)	0.001
Male	138 (56.3)	72 (47.7)	66 (70.2)	
Type of transplant				
Deceased	51 (20.8)	34 (22.5)	17 (18.1)	0.424
Living	194 (79.2)	117 (77.5)	77 (81.9)	
Type of dialysis				
HD	199 (81.2)	120 (79.5)	79 (84)	0.139
PD	30 (12.2)	23 (15.2)	7 (7.4)	
Pre-emptive	16 (6.5)	8 (5.3)	8 (8.5)	
Dialysis vintage*	3.1 ± 3	3.1 ± 3	3 ± 3	0.801
History of HTN	189 (77.1)	103 (68.2)	86 (91.5)	< 0.001
DM	100 (40.8)	40 (26.5)	60 (63.8)	< 0.001
Lipid profile (LDL > 100 mg/dl)	97 (39.6)	66 (43.7)	31 (33)	0.108
Smoking	22 (9)	12 (7.9)	10 (10.6)	0.497
CAD	31 (12.7)	19 (12.6)	12 (12.8)	1
PVD	6 (2.4)	3 (2)	3 (3.2)	0.502
CVD	7 (2.9)	3 (2)	4 (4.3)	0.508
Metabolic changes in the first-year postkidney transplantation				
Creatinine (12 months)*	98 ± 63.1	93.6 ± 63.8	105 ± 61.7	0.170
Graft rejection	19 (7.8)	11 (7.3)	8 (8.5)	0.807
BMI (kg/m²) (pre-KTx)*	25.4 ± 5.7	24.8 ± 5.6	26.3 ± 5.7	0.041
BMI (kg/m²) (12 months)*	27.8 ± 5.8	27.1 ± 5.5	28.8 ± 6.2	0.023
Weight change (kg)*	6.3 ± 8.3	6.1 ± 7.8	6.6 ± 9.1	0.598
HbA1c (increased > 0.5%)	113 (63.8)	65 (61.9)	48 (66.7)	0.529
New-onset DM after KTx (12 months)	20 (8.2)	9 (6)	11 (11.7)	0.149
Persistent hyperparathyroidism	40 (16.3)	27 (17.9)	13 (13.8)	0.479

*Data reported as *n* (%), except for (*) data reported as n ± SD.

CAD, coronary artery disease; CVD, CV disease; DM, diabetes mellitus; HD, hemodialysis; HTN, hypertension; LDL, Low-density lipoprotein; NODAT, new-onset diabetes mellitus after transplantation; PD, peritoneal dialysis; PVD, peripheral vascular disease.

than two antihypertensive medications at 12 months post-KTx. All reported *P*-values are two-sided and *P*-values < 0.05 were considered to indicate a statistical significance. The study was registered on the Research Registry under the unique identifying number research registry 8825. This study is conducted in accordance with the STROCSS criteria[30].

Results

Characteristics of patients

A total of 245 patients post-KTx were included in the study with an average age of 43.2 ± 16, of which 138 (56.3%) were male and 194 (79.2%) were living donor KTx. Pre-emptive KTx was done in 16 patients (6.5%), history of coronary artery disease (CAD) was present in 31 patients (12.7%), diabetes mellitus (DM) was present in 100 patients (40.8%), and 22 patients (9%) were smokers.

In all, 94 patients (38.4%) had greater than or equal to 2 HTN medications, while 151 patients (61.6%) had less than or equal to 1 HTN medication at 1-year post-KTx. Patients who were males ($P=0.001$) or a diabetic ($P<0.001$) were more likely to be taking more antihypertensive medications. Moreover, the body mass index (BMI) pre-KTx (24.8 vs 26.3, $P=0.041$) and at 12 months was significantly higher in the DTC group (27.1 vs 28.8, $P=0.023$).

On the contrary, there were no differences between the two groups of patients in the type of KTx ($P=0.424$), type of dialysis ($P=0.139$), smoking status ($P=0.497$), presence of known CAD ($P=1$), rate of graft rejection ($P=0.807$), BMI change ($P=0.707$), HbA1c increase ($P=0.529$), creatinine level ($P=0.170$), and new-onset diabetes after KTx ($P=0.149$). Persistent hyperparathyroidism, as defined as a parathyroid hormone level greater than 2 times of the normal level, at 6–12 months post-KTx was also similarly distributed in both group ($P=0.479$).

Table 2

Baseline pre-KTx CV imaging

	Total $n=245$ (%)	≤1 HTN medication $n=151$ (%)	≥2 HTN medications $n=94$ (%)	P
Echocardiography findings				
Ejection fraction				
25–35	1 (0.4)	0	1 (1.1)	0.032
35–45	12 (5.1)	6 (4.2)	6 (6.6)	
45–55	34 (14.5)	15 (10.4)	19 (20.9)	
> 55	188 (80)	123 (85.4)	65 (71.4)	
Left ventricular hypertrophy				
Yes	89 (36.3)	46 (30.5)	43 (45.7)	0.051
No	146 (59.6)	98 (64.9)	48 (51.1)	
N.A.	10 (4.1)	7 (4.6)	3 (3.2)	
Wall motion abnormality on echocardiography				
Yes	31 (12.7)	11 (7.3)	20 (21.3)	0.005
No	204 (83.3)	133 (88.1)	71 (75.5)	
N.A.	10 (4.1)	7 (4.6)	3 (3.2)	
Calcium scoring on PET CT scan				
0	54 (22)	38 (25.2)	16 (17)	0.001
1–100	36 (14.7)	19 (12.6)	17 (18.1)	
100–400	19 (7.8)	6 (4)	13 (13.8)	
More than 400	24 (9.8)	10 (6.6)	14 (14.9)	
Not required	112 (45.7)	78 (51.7)	34 (36.2)	
Cardiac perfusion nuclear stress test				
Abnormal perfusion	36 (14.7)	12 (7.9)	24 (25.5)	< 0.001
Normal perfusion	90 (36.7)	49 (32.5)	41 (43.6)	
Not required	119 (48.6)	90 (59.6)	29 (30.9)	
Cardiac catheterization				
CAD present, for coronary intervention	12 (4.9)	1 (0.7)	11 (11.7)	< 0.001
CAD present, for medical treatment	25 (10.2)	8 (5.3)	17 (18.1)	
No CAD	4 (1.6)	4 (2.6)	0	
Not required	204 (83.3)	138 (91.4)	66 (70.2)	
Atherosclerosis on CT				
No atherosclerosis	97 (39.6)	61 (40.4)	36 (38.3)	0.008
Mild	13 (5.3)	4 (2.6)	9 (9.6)	
Moderate/severe	6 (2.4)	1 (0.7)	5 (5.3)	
Not required	129 (52.7)	85 (56.3)	44 (46.8)	

Data reported as *n* (%).

CAD, coronary artery disease; CT, computed tomography; N.A, not applicable; PET, positron emission tomography.

A summary of the patients' findings is listed in Table 1.

Characteristics of baseline CV imaging

Abnormal pre-KTx CV imaging was significantly more common in the DTC group, including reduced ejection fraction <55% (14.6% vs 28.6%, $P=0.032$), presence of left ventricular hypertrophy (30.5 vs 45.7%, $P=0.051$), presence of wall motion abnormality (7.3 vs 21.3% $P=0.005$), calcium scoring >400 (6.6 vs 14.9%, $P=0.001$), abnormal perfusion on the nuclear stress test (7.9 vs 25.5%, $P<0.001$), coronary artery disease on cardiac catheterization (6 vs 29.8%, $P<0.001$) and moderate/severe atherosclerosis on CT (0.7 vs 5.3%, $P=0.008$). All the listed factors were more common in the DTC HTN group Figure 1. Other CV imaging findings are listed in Table 2.

Blood pressure and number of antihypertensive medications

SBP was significantly higher in the group with DTC HTN at baseline (pre-KTx) (143.7 vs 136, $P=0.005$), 1-month post-KTx (141.3 vs 132.7, $P<0.001$), and 12 months post-KTX (138.5 vs 128, $P<0.001$). Similarly, DBP was significantly higher at 1-month (75.5 vs 70.6, $P=0.008$) and 12 months post-KTx (73.9 vs 69.8 vs, $P=0.020$). SBP and DBP of both groups trended down in the first-year post-KTx. These changes of SBP and DBP were not different between the two groups ($P=0.398$ for changes in SBP (0–12 mo) and $P=0.073$ for changes in DBP (0–12 months) (Table 3).

Additionally, after KTx, the number of HTN medications needed in patients with DTC HTN at 12 months were higher than 1-month 'trended up' whereas the number of HTN medications needed decreased in the other group (0.2 vs –0.4 vs, $P<0.001$). Despite the use of more antihypertensive medications in the DTC group, uncontrolled HTN was more prevalent at 1-month (34.4 vs 58.5%, $P<0.001$) and 12 months (20.5 vs 44.7%, $P<0.001$). There were more RAAS inhibitors and statins use in the group with DTC HTN [(13.8 vs1.3%, $P<0.001$) and (80.9 vs 57% vs $P<0.001$), respectively].

Multivariate analysis indicated a relation with age (aOR: 1.027, 95% CI: 1.002–1.051), male gender (aOR: 2.057, 95% CI: 1.096–3.862), baseline DM (aOR: 2.065, 95% CI: 1.005–4.243), baseline HTN (aOR 2.82, 95% CI: 1.131–7.043), and baseline use of greater than or equal to 2 HTN medications (aOR 6.146, 95% CI: 2.367–15.955) (Table 4).

Discussion

BP tends to improve in the following weeks/months following KTx and gets easier to control with a lower number of antihypertensive medications[31,32]. Our study showed similar findings and BP trended down in the first-year post-KTx in both patient groups. The number of antihypertensive medications also decreased in most patients, as time progressed. However, more than one-third of KTRs had DTC HTN and continued to require greater than or equal to 2 HTN medications at 1-year post-KTx. The risk factors of DTC HTN at 1-year post-KTx were age, male sex, presence of DM, HTN pre-KTx, and requiring antihypertensive medications at 1-month post-KTx. KTRs with an abnormal pretransplant cardiac work-up were also more likely to require more antihypertensive medications.

Post-KTx antihypertensive medications are occasionally used for additional indications beside their antihypertensive properties. For example, RAAS inhibitors can be used to control post-KTx polycythemia, α-blockers to control benign prostatic hyperplasia symptoms, and β-blockers for their cardiac remodeling effects[33–35]. This study did not examine the specific indications of each antihypertensive medication. However, the

Table 3

Changes of blood pressure, number of antihypertensive medications, and rate of achieving blood pressure goals

	Total $n=245$	≤1 HTN medication $n=151$	≥2 HTN medications $n=94$	*P*
Changes of blood pressure				
SBP (pre-KTx)	139 ± 21.9	136 ± 23	143.7 ± 19.3	0.005
SBP (1 months)	136 ± 17.7	132.7 ± 17.9	141.3 ± 16	< 0.001
SBP (12 months)	132 ± 14.8	128 ± 13.8	138.5 ± 14	< 0.001
Changes in SBP (0–12 months)	− 6.8 ± 25.3	− 7.9 ± 26.9	− 5.2 ± 22.7	0.398
DBP (pre-KTx)	77.7 ± 15.1	77.7 ± 15.6	77.6 ± 14.3	0.959
DBP (1 months)	73.6 ± 13.4	75.5 ± 11.8	70.6 ± 15.3	0.008
DBP (12 months)	72.3 ± 13.2	73.9 ± 12.3	69.8 ± 14.1	0.020
Change in DBP (0–12 months)	− 5.4 ± 18.3	− 3.8 ± 20.1	− 7.9 ± 14.7	0.073
Changes of number of antihypertensive medications				
≥ 2 medications (1 months)	32 (13.1%)	7 (4.6%)	25 (26.6%)	< 0.001
Number of BP medications (1 months)	1.4 ± 1.1	0.9 ± 0.8	2.1 ± 0.9	< 0.001
Number of BP medications (6 months)	1.2 ± 0.9	0.6 ± 0.6	2.1 ± 0.5	< 0.001
Number of BP medications (12 months)	1.2 ± 1	0.5 ± 0.5	2.3 ± 0.6	< 0.001
Medications change	-0.2 ± 0.9	-0.4 ± 0.7	0.2 ± 1	< 0.001
Medications increased (% patients)	32 (13.1%)	6 (4%)	26 (27.7%)	< 0.001
Rate of uncontrolled BP (> 140/90)				
BP > 140/90 (pre-KTx)	119 (48.8%)	64 (42.7%)	55 (58.5%)	0.018
BP > 140/90 (1 months)	107 (43.7%)	52 (34.4%)	55 (58.5%)	< 0.001
BP > 140/90 (12 months)	73 (29.8%)	31 (20.5%)	42 (44.7%)	< 0.001
Converted to uncontrolled (0–12 months)	37 (17.7%)	19 (13.7%)	18 (25.7%)	0.036

Data reported as n ± SD, except for (*) data reported as *n* (%).

BP, blood pressure; DBP, diastolic blood pressure; SBP, systolic blood pressure.

Table 4

Multivariate analysis of the risk factors of a higher need for antihypertensive medications at 12 months post-KTx

	aOR	95% CI	*P*
Age	1.027	1.002–1.051	0.031
Male vs. female	2.057	1.096–3.862	0.025
History of HTN	2.822	1.131–7.043	0.026
DM	2.065	1.005–4.243	0.048
Antihypertensive medications ≥ 2 at 1 month post-KTx	6.146	2.367–15.955	<0.001

DTC HTN group remained with higher BP values and suboptimal BP control at 1-year post-KTx, despite the use of a higher number of antihypertensive medications.

This indicates that KTRs with abnormal baseline cardiac work-up are less likely to attain their BP targets at 1-year post-KTx in spite of additional antihypertensive medication. Subsequently, this group requires close attention to their antihypertensive management especially due to their higher CV risk. Additionally, requiring greater than or equal to 2 antihypertensive medications at one month post-KTx is a predictor of DTCHTN at 1-year post-KTx. Similar findings were observed in other studies[36,37]. These results suggest that these KTRs may require early titration of their antihypertensive management upon follow-ups.

Obesity is also an important factor of DTC HTN in the general population[38–41] and post-KTx systolic HTN[42]. KTRs with DTC HTN had a higher pre-KTx BMI and at 12 months post-KTx but both groups gained weight in a similar fashion. Preventing and treating obesity among KTRs may reduce their antihypertensive medications burden[43,44].

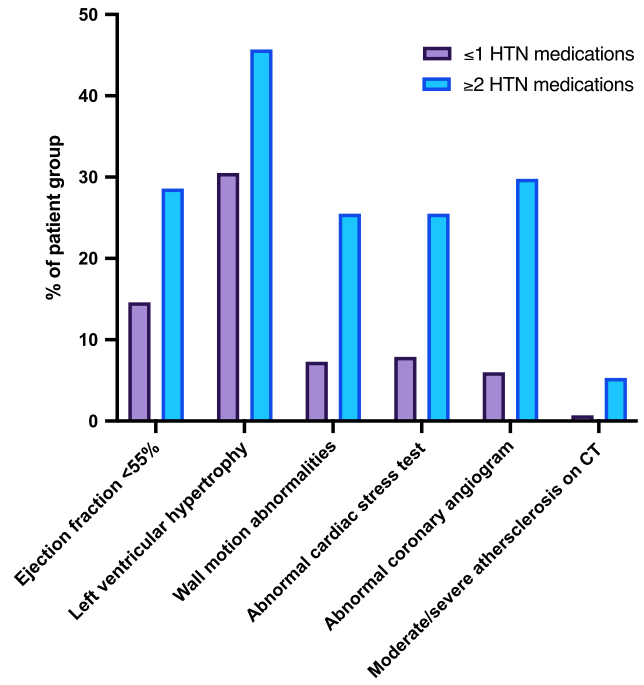

Figure 1. Abnormal CV imaging findings in patients with difficult-to-control hypertension versus other patients.

Our study showed no relation between the number of antihypertensive medications and other baseline factors (e.g. dialysis vintage or dialysis type), or post-KTx factors (graft function, rejection, or glycemic control). Though we cannot rule out a lack of representation due to the sample size.

This single-center retrospective study has several limitations. This study examined BP readings only at four intervals and did not specify the classes of antihypertensive medications. Additionally, compliance was not verified except through medications refills. Nonetheless, this study is unique as the association between antihypertensive medications and post-KTx metabolic changes and cardiac work-up was never studied before. It highlights the need for more aggressive antihypertensive regimen in KTRs with abnormal baseline CV imaging.

Conclusion

In summary, this study provides a current overview of the different factors associated with post-KTx DTC HTN. According to our findings, DTC HTN patients were more likely to be older, males, diabetics, previously hypertensive, on greater than or equal to 2 antihypertensive medications at 1-month post-KTx, and to have abnormal baseline pre-KTx CV imaging. These patients require special attention when addressing their HTN. Further prospective, controlled trials are necessary to further evaluate these findings.

Ethics approval

The King Abdullah International Medical Research Center institutional review board (IRB) approved this study (NRC21R/390/09). Patient consent was waived due to the nature of the study.

Consent to participate

Not applicable.

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This study did not receive funding from any source.

Authors' contributions

All authors contributed to the research and/or preparation of the manuscript. All authors read and approved the final manuscript.

Conflicts of Interest disclosure

The authors declare no conflict of interest.

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References

[1] Aakhus S, Dahl K, Widerøe TE. Cardiovascular disease in stable renal transplant patients in Norway: morbidity and mortality during a 5-yr follow-up. Clinical Transplantation 2004;18:596–604.
[2] Matas AJ, Gillingham KJ, Humar A, *et al*. 2202 kidney transplant recipients with 10 years of graft function: what happens next. American Journal of Transplantation 2008;8:2410–9.
[3] Weir MR, Burgess ED, Cooper JE, *et al*. Assessment and management of hypertension in transplant patients. Journal of the American Society of Nephrology 2015;26:1248–60.
[4] Alexandrou M-E, Ferro CJ, Boletis I, *et al*. Hypertension in kidney transplant recipients. World Journal of Transplantation 2022;12:211–22.
[5] Opelz G, Wujciak T, Ritz E. Association of chronic kidney graft failure with recipient blood pressure. Collaborative Transplant Study Kidney Int 1998;53:217–22.
[6] Pagonas N, Bauer F, Seibert FS, *et al*. Intensive blood pressure control is associated with improved patient and graft survival after renal transplantation. Sci Rep 2019;9:10507.
[7] Chatzikyrkou C, Menne J, Gwinner W, *et al*. Pathogenesis and management of hypertension after kidney transplantation. J Hypertens 2011;29:2283–94.
[8] Zeier M, Mandelbaum A, Ritz E. Hypertension in the transplanted patient. Nephron 1998;80:257–68.
[9] A randomized clinical trial of cyclosporine in cadaveric renal transplantation. New England Journal of Medicine 1986;314:1219–25.
[10] Miller LW. Cardiovascular toxicities of immunosuppressive agents. American Journal of Transplantation 2002;2:807–18.
[11] Hamrahian SM, Falkner B. Hypertension in chronic kidney disease. Adv Exp Med Biol 2017;956:307–25.
[12] Hricik DE. Metabolic syndrome in kidney transplantation: management of risk factors. Clin J Am Soc Nephrol 2011;6:1781–5.
[13] Bruno S, Remuzzi G, Ruggenenti P. Transplant renal artery stenosis. J Am Soc Nephrol 2004;15:134–41.
[14] Agarwal R, Alborzi P, Satyan S, *et al*. Dry-weight reduction in hypertensive hemodialysis patients (DRIP). Hypertension 2009;53:500–7.
[15] Kasiske BL, Anjum S, Shah R, *et al*. Hypertension after kidney transplantation. Am J Kidney Dis 2004;43:1071–81.
[16] Kubo MN, Kayima JK, Were AJ, *et al*. Changes in blood pressure levels and antihypertensive medication use before and after renal transplantation among patients in nairobi, kenya: a comparative cross-sectional study. International Journal of Hypertension 2016;2016:1–5.
[17] Midtvedt K, Hartmann A, Bentdal Ø, *et al*. Bilateral nephrectomy simultaneously with renal allografting does not alleviate hypertension 3 months following living-donor transplantation. Nephrology Dialysis Transplantation 1996;11:2045–9.
[18] Małyszko J, Małyszko J, Bachórzewska-Gajewska H, *et al*. Inadequate blood pressure control in most kidney transplant recipients and patients with coronary artery disease with and without complications. Transplantation Proceedings 2009;41:3069–72.
[19] Kaul A, Sharma RK, Gupta A, *et al*. Spectrum of hypertension in post transplant. J Assoc Physicians India 2010;58:221–4.
[20] Visco V, Finelli R, Pascale AV, *et al*. Difficult-to-control hypertension: identification of clinical predictors and use of ICT-based integrated care to facilitate blood pressure control. Journal of Human Hypertension 2018;32:467–76.
[21] Viera AJ, Hinderliter AL. Evaluation and management of the patient with difficult-to-control or resistant hypertension. Am Fam Physician 2009;79:863–9.
[22] Carey RM, Calhoun DA, Bakris GL, *et al*. Resistant hypertension: detection, evaluation, and management: a scientific statement from the american heart association. Hypertension 2018;72:e53–90.
[23] Midtvedt K, Hartmann A. Hypertension after kidney transplantation: are treatment guidelines emerging. Nephrology Dialysis Transplantation 2002;17:1166–9.
[24] Aziz F, Clark D, Garg N, *et al*. Hypertension guidelines: How do they apply to kidney transplant recipients. Transplantation Reviews 2018;32:225–33.
[25] Arabi Z, Theaby A, Sibai A, *et al*. Consensus guidelines of cardiovascular risk assessment in kidney transplantation in Saudi Arabia: review of current practice, evidence, and recommendations. Saudi J Kidney Dis Transpl 2020;31:655–75.
[26] Lentine KL, Costa SP, Weir MR, *et al*. Cardiac disease evaluation and management among kidney and liver transplantation candidates. Circulation 2012;126:617–63.
[27] Arabi Z, Theaby A, Farooqui M, *et al*. The national guard health affairs guidelines for the medical management of renal transplant patients. Special Article Saudi Journal of Kidney Diseases and Transplantation 2018;29:1452–69.
[28] Taler SJ, Agarwal R, Bakris GL, *et al*. KDOQI US Commentary on the 2012 KDIGO clinical practice guideline for management of blood pressure in CKD. American Journal of Kidney Diseases 2013;62:201–13.
[29] Agha R, Abdall-Razak A, Crossley E, *et al*. STROCSS 2019 guideline: strengthening the reporting of cohort studies in surgery. Int J Surg 2019;72:156–65.
[30] Mathew G, Agha R, Albrecht J, *et al*. STROCSS 2021: strengthening the reporting of cohort, cross-sectional and case-control studies in surgery. International Journal of Surgery Open 2021;96:106165.
[31] Rossi AP, Vella JP. Hypertension, living kidney donors, and transplantation: where are we today. Adv Chronic Kidney Dis 2015;22:154–64.
[32] Paoletti E, Gherzi M, Amidone M, *et al*. Association of arterial hypertension with renal target organ damage in kidney transplant recipients: the predictive role of ambulatory blood pressure monitoring. Transplantation 2009;87:1864–9.
[33] Hiremath S, Fergusson D, Doucette S, *et al*. Renin angiotensin system blockade in kidney transplantation: a systematic review of the evidence. Am J Transplant 2007;7:2350–60.
[34] Opelz G, Döhler B. Cardiovascular death in kidney recipients treated with renin-angiotensin system blockers. Transplantation 2014;97:310–5.
[35] Stoumpos S, Jardine AG, Mark PB. Cardiovascular morbidity and mortality after kidney transplantation. Transpl Int 2015;28:10–21.
[36] Woźniak I, Kolonko A, Chudek J, *et al*. Influence of Polypharmacy on the quality of life in stable kidney transplant recipients. Transplantation Proceedings 2018;50:1896–9.
[37] Bril F, Castro V, Centurion IG, *et al*. A systematic approach to assess the burden of drug interactions in adult kidney transplant patients. Curr Drug Saf 2016;11:156–63.
[38] Jordan J, Yumuk V, Schlaich M, *et al*. Joint statement of the European Association for the Study of Obesity and the European Society of Hypertension: obesity and difficult to treat arterial hypertension. J Hypertens 2012;30:1047–55.
[39] Landsberg L, Aronne LJ, Beilin LJ, *et al*. Obesity-related hypertension: pathogenesis, cardiovascular risk, and treatment–a position paper of the The Obesity Society and The American Society of Hypertension. Obesity (Silver Spring) 2013;21:8–24.
[40] Khan JR, Biswas RK, Islam MM. Relationship between blood pressure and BMI in young adult population: a national-level assessment in Bangladesh. Br J Nutr 2022;128:2075–82.
[41] Jordan J, Boye SW, Breton SL, *et al*. Antihypertensive treatment in patients with class 3 obesity. Ther Adv Endocrinol Metab 2012;3:93–8.
[42] Tantisattamo E, Leelaviwat N, Polpichai N, *et al*. Post-kidney transplant visit-to-visit body mass index variability as a risk of post-transplant systolic hypertension. Current Developments in Nutrition 2020;4:4141693.
[43] John EG, Domingo LT. Hypertension and obesity after pediatric kidney transplantation: management based on pathophysiology: a mini review. Int J Prev Med 2014;5(suppl 1):S25–38.
[44] Tantisattamo E, Molnar MZ, Ho BT, *et al*. Approach and management of hypertension after kidney transplantation. Front Med (Lausanne) 2020;7:229.