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Blood Pressure Treatment in Kidney Transplant Recipients—Can We Improve?

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Background. Hypertension in kidney transplant (KTx) recipients is common, affecting both patient and graft survival. Annual data from the Norwegian Renal Registry reveal that <50% of adult (>18 y) KTx recipients reach target blood pressure (BP) ≤130/80 mm Hg. The aim of this study was to identify the determinants of failure to achieve BP control. **Methods.** In conjunction with the 2018 annual data reporting, additional questions were added for recipients with BP >130/80 mm Hg (treating physician´s target BP for each patient, reasons for not achieving target, method of measurement). **Results.** Annual forms were received from 98% (3407 of 3486) of KTx recipients, with 1787 (52%) reporting a BP >130/80 mm Hg ("above-target" group). These recipients were older, mostly male, with higher body mass index and serum creatinine levels ($P < 0.05$) compared with patients with controlled hypertension ("on-target" group). Valid survey answers were available for 84% of the "above-target" group ($Surv_{resp}$) with no significant demographic differences versus nonresponders ($Surv_{nonresp}$). Among $Surv_{resp}$, 32% were under antihypertensive dose titration, whereas dose-limiting side effects were reported in 7%. Target BP was confirmed to 130/80 mm Hg for 60% of $Surv_{resp}$. In recipients for whom the treating physician set target BP >130/80 mm Hg, 51% did not reach these individual targets. The number of antihypertensive drugs was significantly higher in the "above-target" group versus "on-target" group (mean 2.1 ± 1.2 versus 1.8 ± 1.3) and 36% versus 25% used ≥3 antihypertensive drugs ($P < 0.05$). Automatic attended BP measurement was utilized by 51%. **Conclusions.** In KTx recipients, a higher BP target achievement seems possible, potentially in the range of 75%-80%.

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Kidney transplantation (KTx) is the preferred treatment for patients with kidney failure, leading to increased patient survival and improved quality of life compared with dialysis.[1-5] Despite successful transplantation, cardiovascular (CV) disease remains the leading causes of increased mortality and the main nonimmunological reason for graft loss.[6,7]

Posttransplant hypertension is common with a reported prevalence of 50%-90%,[8-10] and an important risk factor for CV complications and reduced graft function.[11,12]

Observational studies by Opelz and Döhler[13] reported a stepwise improvement in both graft and patient survival associated with lower blood pressure (BP). A similar tendency was reported for systolic BP by Carpenter et al[14] who assessed the possible association between BP and CV disease in a post hoc analysis of participants in the Folic Acid for Vascular Outcome Reduction In Transplantation trial. They found that each 20-mm Hg increase in systolic BP was associated with a 32% increase in the risk of CV events.

A consensus on a specific BP target for KTx recipients has, however, not been clearly specified.[15,16] Based on the available literature, the Norwegian Renal Registry (NRR) has adapted the Kidney Disease Improving Global Outcomes (KDIGO)

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guideline BP target of ≤130/80 mm Hg for adult (>18 y) KTx recipients.[17] The NRR is a national medical quality registry designed to facilitate optimized treatment for all KTx recipients in Norway. The NRR has set the overall target of 80% of patients to achieve the guideline BP, accepting that some patients will not reach the BP target (drug side effects, resistant hypertension, nonadherence).

Historically the target BP goal has been achieved by <50% of patients in the NRR (Figure 1).[18] Therefore, in the 2018 return, a short survey focusing on recipients with BP >130/80 mm Hg was distributed (Figure 2) along with the annual capture of individual data by the NRR. The aim of this project was to understand treatment decisions and determine the reasons for failure to achieve the BP target.

MATERIALS AND METHODS

As a national medical registry, the NRR collects data on all KTx recipients in Norway on an annual basis. The NRR has complete coverage of all kidney transplants in Norway since the late 1960s and annual data has been collected since 1994. The annual reports are collected on paper forms and include information regarding complications, current medication (eg, immunosuppressive drugs, antihypertensives, antithrombotics), clinical chemistry, weight, BP, and rejection episodes for each individual patient. Data from the last consultation of the year are reported to the registry by the treating physician. BP should be measured according to center practice, with the recommended value being mean of the second and third measurements following a 5-min rest period. Proteinuria was defined as albumin to creatinine ratio (ACR) >30 mg/g and/or protein to creatinine ratio (PCR) >50 mg/g. In recent decades the response rate for annual data has been 96% to 98% and in conjunction with the capture of annual data for 2018, additional information was requested for recipients with a systolic BP >130 mm Hg and/or diastolic BP >80 mm Hg.

This was a quality assessment study for the NRR, approved by the hospital Data Protection Officer.

The Survey

The survey, together with the annual forms, was distributed by mail to the reporting centers in January 2019. They were to be answered and returned by April 1, 2019. Survey questions are presented in Figure 2. The survey also included a free-text field for general comments.

Statistical Analysis

Survey-information was tabulated and descriptive statistics were performed using the Statistical Package for the Social Sciences version 26.0.0.1 (IBM Corp, Armonk, NY). A 2-tailed *P* value of <0.05 was considered statistically significant. Data are presented as mean and SD or 95% confidence interval.

RESULTS

By the end of 2018, there were a total of 3486 adult (>18 y old) KTx recipients alive with functioning grafts. The overall response rate in the 2018 annual return was 98% (3407 of 3486) (Figure 3). The population demographic and clinical characteristics are shown in Table 1. Fifty-two percent (1787 of 3407) of the recipients had a BP >130/80 mm Hg, representing the study population for which additional survey data were requested. The BP survey response rate was 84% (1500 of 1787) ($Surv_{resp}$); the 287 recipients with BP >130/80 mm Hg for whom no survey data were received are referred to as $Surv_{nonresp}$.

The "above-target" patients (n = 1787) were significantly older, more often male, with higher body mass index (BMI) and serum creatinine compared with the "on-target" patients (n = 1620) (Table 1) and with more recent transplants. As anticipated, the "above-target" patients were prescribed higher number of antihypertensive agents and the use of angiotensin-converting-enzyme inhibitors (ACEis) or angiotensin

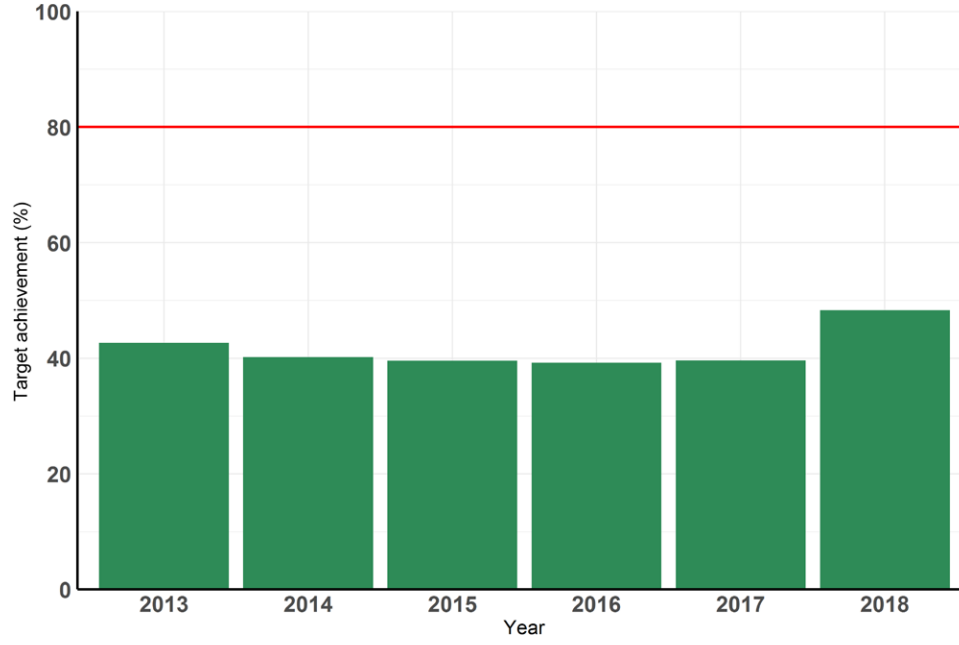

FIGURE 1. Kidney transplant recipients in the Norwegian Renal Registry with blood pressure ≤130/80 mm Hg by reporting y.

What is, in your clinical assessment, the patient's target blood pressure?

…… / ……. mmHg

Is medication udner increasement?

☐ Yes
☐ No

If registered blood pressure is above your clinical assessment of target blood pressure, what are the reason(s) for no further increase in medcation?

(choose one or more of the following options)

☐ registered blood pressure is not representative for the patients average blood pressure level
☐ trouble with adherence/compliance
☐ side effects of antihypertensives
☐ postural hypotention
☐ other cause: ……

Method of measurement

☐ Manually
☐ Automatic ☐ attended ☐ non-attended
☐ 24-hour

Comment: ……

FIGURE 2. The survey issued by the Norwegian Renal Registry should be answered for patients with a measured systolic blood pressure >130 mm Hg and/or a diastolic blood pressure >80 mm Hg.

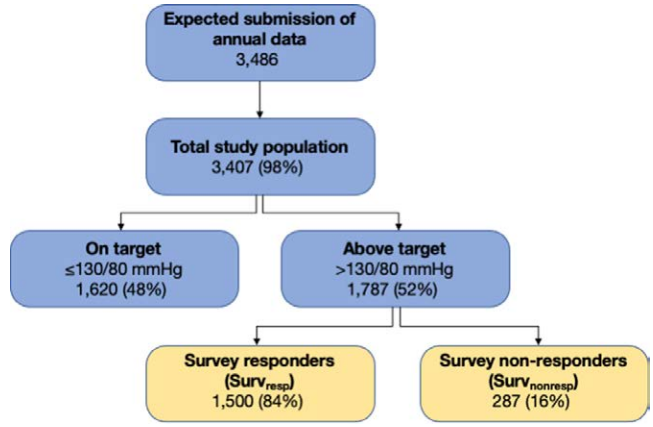

FIGURE 3. Flowchart over the submission of annual data from adult (>18 y) kidney transplant recipients to the Norwegian Renal Registry and survey response in 2018. Surv$_{nonresp}$, survey nonresponders for "above-target" group; Surv$_{resp}$, survey responders for "above-target" group.

receptor blockers (ARBs) was greater than in the "on-target" group (Table 1). Diabetes before transplantation was present in 18% in the "above-target" group versus 17% in the "on-target" group (Table 1). ACR and/or PCR was reported in 92% of patients; 17% of the entire cohort had proteinuria, 21% in the "above-target" group compared with 13% in the "on-target" group ($P < 0.001$). Patients treated with ACEi/ARB were more likely to have proteinuria (21% versus 14%; $P < 0.001$) with the highest use being in the "above-target" group (23%). There were no significant demographic differences of importance for the development of hypertension between the Surv$_{resp}$ versus Surv$_{nonresp}$ groups (Table 1).

Mean BP for the "above-target" group was 140 ± 13/82 ± 9 mm Hg with systolic BP ranging from 109 to 220 mm Hg and diastolic from 49 to 118 mm Hg. Elevated systolic and diastolic pressure (>130/>80 mm Hg) were present in 40% (603 of 1500) (Table 2).

Individual BP targets were reported for 94% (1413 of 1500) of the Surv$_{resp}$ patients. In 60% (847 of 1413), the treating physician reported 130/80 mm Hg as the target BP. Some reported isolated lower systolic (4%) or diastolic (5%) target BP. The remaining 36% (n = 504) reported a higher target BP, and 51% (256 of 504) of these patients did not reach this higher treatment target. The 2 main reasons given by treating physician reporting a higher individual BP target were side effects from antihypertensive medication (27%) and postural hypertension (20%).

For 82% of the patients with a reported BP target (1162 of 1413), the treating physicians stated a lower individual target than the patients' actual reading. One-third of the Surv$_{resp}$ patients (485 of 1500) were under active antihypertensive dose titration (Table 2). In the Surv$_{resp}$ patients not undergoing dose titration, the main reason for not intensifying the treatment was that the reported BP was not representative

TABLE 1.

Demographic and clinical characteristics of kidney transplant study population by the end of 2018

Variable	All (n = 3407)	"On-target" (n = 1620)	"Above-target" (n = 1787)			
			$Surv_{resp}$ (n = 1500)	$Surv_{nonresp}$ (n = 287)	*P* $Surv_{resp}$ vs $Surv_{nonresp}$	*P* on-target vs $Surv_{resp}$
Age (y)	58 ± 14	57 ± 15	59 ± 14	59 ± 14	0.70	0.008
Male gender	2185 (64)	1009 (62)	988 (66)	188 (66)	0.91	0.03
BMI (kg/m^2)	27 ± 5	26 ± 5	27 ± 5	27 ± 5	0.99	0.001
Years after Tx	10.4 ± 8.1	10.8 ± 8.5	9.9 ± 8.0	10.4 ± 8.1	0.36	0.002
Immunosuppression						
Tacrolimus	2117 (62)	998 (62)	948 (63)	171 (60)	0.25	0.54
Cyclosporine A	1029 (30)	490 (30)	449 (30)	90 (31)	0.63	0.96
Mycophenolate	2769 (81)	1311 (81)	1238 (83)	220 (77)	0.03	0.62
Prednisolone	3342 (98)	1594 (98)	1467 (98)	281 (98)	0.91	0.22
Other[a]	457 (13)	222 (14)	183 (12)	52 (18)	0.15	0.21
Antihypertensives	1.9 ± 1.3	1.8 ± 1.3	2.1 ± 1.2	2.0 ± 1.3	0.30	<0.001
0	417 (12)	256 (16)	134 (9)	27 (9)	0.80	<0.001
1	891 (26)	454 (28)	359 (24)	78 (27)	0.26	0.02
2	896 (26)	395 (24)	418 (28)	83 (30)	0.72	0.02
3	674 (20)	275 (17)	344 (23)	55 (19)	0.14	<0.001
≥4	369 (11)	139 (9)	194 (13)	36 (12)	0.86	<0.001
Missing	160 (5)	101 (6)	51 (3)	8 (3)		
ACEi/ARB	1450 (43)	640 (40)	694 (46)	116 (40)	0.08	0.001
P-creat (μmol/L)	130 ± 63	126 ± 58	135 ± 68	131 ± 66	0.38	<0.001
Proteinuria[b]	537 (17)	195 (13)	289 (21)	53 (20)	0.85	<0.001
Missing	282 (8)	144 (9)	112 (7)	26 (9)		
Complications[c]	291 (9)	124 (8)	162 (11)	5 (2)	<0.001	0.08

[a]Other immunosuppression: azathioprine, everolimus, sirolimus, and belatacept.
[b]Proteinuria defined as ACR >30 mg/g and/or PCR >50 mg/g.
[c]Complications = myocardial infarction, stroke, coronary surgery/PCI, and other heart surgery.
Data are presented as mean ± SD and n (%).
ACEi, angiotensin-converting-enzyme inhibitor; ACR, albumin to creatinine ratio; ARB, angiotensin receptor blocker; BMI, body mass index; PCI, percutaneous coronary intervention; PCR, protein to creatinine ratio; P-creat, plasma creatinine; $Surv_{nonresp}$, survey nonresponders for "above-target" group; $Surv_{resp}$, survey responders for "above-target" group; Tx, transplantation.

of the patient´s average BP during preceding year (28%, 427 of 1500) and 24% (361 of 1500) reported other causes; for 136 patients, the physicians considered the patients BP as adequate (78 of these patients had a BP <135/85 mm Hg), 28 had comorbidities limiting treatment, and 22 patients had "white coat" hypertension (Table 2). Postural hypotension (10%, 154 of 1500), other side effects of antihypertensive drugs (7%, 105 of 1500), and nonadherence (4%, 62 of 1500) were also reported as reasons for the decision not to up-titrate antihypertensive therapy.

On average, patients´ in the $Surv_{resp}$ group used 2.1 antihypertensive agents (Table 1): 75% (1121 of 500) were on 1-3 antihypertensive drugs, 36% (538 of 1500) used ≥3 agents, and 9% (134 of 1500) were not using any antihypertensive medication (Table 1).

Direct automatic measurement of BP was most frequently method of BP monitoring (51%, 773 of 1500), whereas manual measurement was conducted by 31% (460 of 1500). Automatic, nonattended measurement was performed by 10% (150 of 1500) and ambulatory 24-h BP was the main method reported by 3% (42 of 1500).

The majority in the $Surv_{resp}$ group were on triple immunosuppression with calcineurin inhibitors (CNIs; tacrolimus or cyclosporine) (93%), mycophenolate (83%), and prednisolone (98%) (Table 1). Three agent immunosuppression including CNI was reported for 74% (1196 of 1620) of the "on-target" group and 70% (201 of 287) of the $Surv_{nonresp}$ group. There were no statistically significant differences in immunosuppressive medication between the "on-target" and the "above-target" group. However, the usage of statins was somewhat higher in the "above-target" group; 74% (1103 of 1500) versus 70% (1132 of 1620) ($P = 0.015$).

Any CV complication, specified as myocardial infarction, stroke, coronary surgery, percutaneous coronary intervention, or other heart surgery during the preceding year is part of the annual data reported to the NRR. In 2018, there were a total of 291 reported CV events; 11% (167 of 1500) in the "above-target" group versus 8% (124 of 1620) in the "on-target" group ($P = 0.077$) (Table 1).

DISCUSSION

Our national registry survey on KTx recipients' shows that 52% did not reach BP target (set by the registry at ≤130/80 mm Hg) in 2018. If 1 includes individualized BP targets reported in the survey, the overall target achievement was 55% and excluding those under dose titration resulted in 63% achieving their target BP. Given that hypertension is an established risk factor for CV events and graft survival, it was surprising that only one-third of the "above-target" group was under active antihypertensive dose titration and 9% were actually not on any antihypertensive drugs.

The lack of randomized controlled trials of "optimal BP target" in KTx recipients was recognized by KDIGO when they set a BP target of ≤130/≤80 mm Hg[17] and recommended lower target in patients with proteinuria. Data from publications focusing on posttransplant hypertension and registry data indicate that a minority of KTx recipients achieve the

TABLE 2.

Survey results on measured blood pressure, method of measurement, antihypertensive dose titration, and cause of no antihypertensive dose titration in the "above-target" group with survey response ($Surv_{resp}$)

Survey variable	$Surv_{resp}$ (n = 1500)
Measured blood pressure	
Systolic blood pressure (mm Hg)	109-220 mm Hg (139.8 ± 13.0)
Diastolic blood pressure (mm Hg)	49-118 mm Hg (82.2 ± 9.2)
Elevated systolic and diastolic blood pressure[a]	603 (40)
Isolated elevated systolic blood pressure[a]	565 (38)
Isolated elevated diastolic blood pressure[a]	329 (22)
Method of blood pressure measurement	
Manual	460 (31)
Automatic attended	773 (51)
Automatic nonattended	150 (10)
24-h ambulatory	42 (3)
Missing	75 (5)
Antihypertensive dose titration	
Yes	485 (32)
No	981 (65)
Missing	34 (2)
Cause for no antihypertensive dose titration	
Registered blood pressure not representative	427 (28)
Adherence	62 (4)
Side effects	105 (7)
Postural hypotension	154 (10)
Other	361 (24)

[a]According to guidelines ≤130/80 mm Hg.
Data are presented as range, mean ± SD, and n (%).
$Surv_{resp}$, survey responders for hypertensive patients (n = 1500).

KDIGO BP target.[8,18,19] There are several other international hypertension guidelines advocating a more relaxed BP target for nonproteinuric patients with chronic kidney disease of <140 mm Hg.[20,21] However, even with this target, 36% of our hypertensive KTx recipients had a systolic BP >140 mm Hg raising the question why nephrologists involved in renal transplant management appear to settle for a higher-than-recommended BP for many patients? It is possible that treating physicians accept reaching either the systolic or the diastolic BP target level (if the other is fairly close) and, in support of this notion, only 40% of patients who did not reach the BP goal failed to reach both systolic and diastolic goal.

The current study reveals that the recipients in the "above-target" group were significantly older (59 ± 14 versus 57 ± 15 y; $P < 0.05$), more likely to be male, with a higher BMI and serum creatinine when compared with the "on-target" group. These are all traditional risk factors for the development of hypertension and confirm previous reports in transplant patients.[8,10,11] In 56% of cases, the reporting physicians confirmed use of the NRR target BP ≤130/≤80 mm Hg. In 36% of responses, the treating physician set a higher individual target BP than 130/80 mm Hg, despite which 51% of their KTx recipients failed to reach the higher treatment target. Overall, 82% (1162 of 1413) of the $Surv_{resp}$ group had a reported BP the treating physician considered "not acceptable." Despite this, only one-third of patients were under active antihypertensive dose up-titration and the mean number of antihypertensive drugs was only 2.1. Furthermore, 9% of the "above-target" recipients did not receive any antihypertensive drug therapy. These data suggest that more KTx recipients may reach their BP target simply by increasing the prescription of antihypertensive medication.

In the $Surv_{resp}$ group, 30% (538 of 1500) used ≥3 antihypertensive agents and are therefore classified as treatment resistant.[22,23] In this group, the median age was 62 y (ranging from 20 to 85 y), 70% were male, the BMI was 28 (16-53) kg/m^2, and serum creatinine level 152 ± 80 µmol/L. With regard to BP in the patients with resistant hypertension, 55% had a systolic BP ≥140 mm Hg and 17% had a diastolic BP ≥90 mm Hg. In this subgroup, improved BP is, if possible, strongly recommended.[13,24] The reasons for not increasing antihypertensive therapy in the present study include in 24% (127 of 538) the statement that the measured BP was not representative for the patients' average BP, postural hypotension limiting dose escalation in 13% (72 of 538), limiting side effects in 10% (56 of 538), and poor adherence in 9% (20 of 538). Overall, these patients account for 16% of the survey population and provide an acceptable reason for setting the target for achieving BP target level of 80% of the total population, a strategy common in most published guidelines.

It is generally recognized that optimal BP control is more important than the use of a specific choice of antihypertensive drug class.[8] In the registry, we have information on the usage of ACEi or ARBs, drugs that have established nephron-protective and antiproteinuric effects in nontransplant populations. In a KTx recipient, specifically in the early postoperative phase, the introduction of blockers of the renin-angiotensin system is often associated with a reduction in glomerular filtration rate, which may be misinterpreted as a rejection episode, which may limit the use. However, in the maintenance phase following transplantation, ACEi/ARBs are excellent antihypertensive drugs with few patient-reported side effects. Overall, in our adult KTx study population, the mean number of antihypertensive drugs was 1.9 ± 1.3 with only 12% not requiring antihypertensive therapy. As expected, the $Surv_{resp}$ were in need of significantly more antihypertensive drugs than the "on-target" group. Moreover, there was a higher prevalence of ACEi/ARB usage in the "above-target" group compared with the "on-target" group ($P = 0.001$). Data were available on the presence or absence of proteinuria (defined as ACR <30 and/or PCR >50) in 92% of the patient with 16% reporting the presence of proteinuria. There were significantly more patients with proteinuria in the "above-target" (21%) versus "on-target" group (13%). The highest prevalence of treatment with an ACEi or an ARB was in the "above-target" group (23%), consistent with an active selection of these drug classes in patients with proteinuria. Unfortunately, the survey has no data on other antihypertensive drug classes.

In an attempt to optimize any drug treatment, identifying patients with adherence problems is important. In KTx recipients, a degree of nonadherence towards immunosuppressive medication is reported to be in the range of 30%-35% and similar findings are likely for antihypertensive medication.[25] Several factors can contribute to nonadherence; hypertension is asymptomatic and medication has side effects, low health literacy, polypharmacy, forgetfulness, and poor physician-patient relationship (including the failure to consider nonadherence).[26] Low adherence was, however, only reported for 4% in the $Surv_{resp}$ group, which we believe reflects underreporting by the treating physicians. Adherence rates have a tendency to fall when the number of drugs increase and higher

adherence to antihypertensive medication has been associated with improved BP control.[27] Regular feedback, patient education, frequent clinic visits, and medication reminder packaging has been shown to improve adherence.[26,28] By performing the survey, we increased the physicians' awareness on BP target, and it will be of interest to see whether BP control is improved in future surveys.

Our cross-sectional survey revealed that the "above-target" group, especially the treatment-resistant subgroup, had a significantly higher BMI than the "on-target" group. A recently published German study (KTx360°) evaluated pre- and post-KTx BMI in 433 recipients.[29] In the present study, 23% versus 19% had a BMI >30 kg/m^2 in the "above-target" and "on-target" groups, respectively ($P = 0.014$). Nonpharmacologic interventions such as diet, exercise, and weight reduction (if warranted) should always be part of posttransplant hypertension treatment. From a clinical perspective, helping the overweight patient with a tailored intervention for weight loss may be even more effective than adding additional antihypertensive drugs.

In the survey, automatic witnessed BP measurement was registered for 51%, whereas 31% was subjected to manual BP measurements. In only 10% of the patients, the physician took the time to use automatic nonattended BP measurements. A recently published study by Mallamaci et al[30] utilizing 24-h ambulatory BP monitoring found that "white coat hypertension" occurred in 12% and masked hypertension in 26% of their KTx patients. However, only 3% of treating physicians had utilized this method of BP monitoring, this despite the fact that 28% of physicians reported that "measured BP is not representative for the patient's average blood pressure." This highlights the need for standardization of BP monitoring, specifically to compare registry outcomes.

The survey only detected a tendency towards more CV incidence in the hypertensive patients during the last year ($P = 0.077$). If we merge CV incidents for the last 3 y, the rates are significantly lower in the "on-target" group (data not shown), supporting the case for intensified BP treatment.

Our study has several limitations. BP measurements were not standardized and reported only on 1 occasion. It is also a weakness that BP data were reported by the treating physician and not blinded. There are no data on smoking, diet (eg, sodium intake), or exercise habits. We only have limited information on the number of antihypertensive drugs and usage of ACEi/ARB, and there is limited information regarding the presence or treatment of hypertension before transplantation (collected since 2016). Information regarding the history of hypertension in deceased donors is also lacking, although there are data from living donors. Our transplant-population is predominantly Caucasian and data may not be representative for patients of other ethnicities. There was also a very large difference between centers in actual BP target achievements ranging from 21% to 81% (data not shown). Currently, the registry data cannot explain the success of 1 center over another, but this shows the potential to improve target achievement. The major strength of our study is the annual capture of data from 98% of the total national population, with the added strength that all patients were transplanted at 1 center with uniform immunosuppressive protocols and CNI target trough levels during follow-up.

In conclusion, our data suggest that in KTx recipients, current BP control is suboptimal, with potential for improved target achievement potentially in the range of 75%-80%. Individualized BP targets based on patient´s comorbidities, age, and other variables might be beneficial in some recipients, as may addressing the reasons for failure to up-titrate therapy and the standardization of BP monitoring.

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REFERENCES

1. Wolfe RA, Ashby VB, Milford EL, et al. Comparison of mortality in all patients on dialysis, patients on dialysis awaiting transplantation, and recipients of a first cadaveric transplant. *N Engl J Med*. 1999;341:1725–1730.
2. Kramer A, Pippias M, Noordzij M, et al. The European Renal Association - European Dialysis and Transplant Association (ERA-EDTA) Registry Annual Report 2015: a summary. *Clin Kidney J*. 2018;11:108–122.
3. Lønning K, Heldal K, Bernklev T, et al. Improved health-related quality of life in older kidney recipients 1 year after transplantation. *Transplant Direct*. 2018;4:e351.
4. Oniscu GC, Brown H, Forsythe JL. How great is the survival advantage of transplantation over dialysis in elderly patients? *Nephrol Dial Transplant*. 2004;19:945–951.
5. Bottomley MJ, Harden PN. Update on the long-term complications of renal transplantation. *Br Med Bull*. 2013;106:117–134.
6. Arend SM, Mallat MJ, Westendorp RJ, et al. Patient survival after renal transplantation; more than 25 years follow-up. *Nephrol Dial Transplant*. 1997;12:1672–1679.
7. Stoumpos S, Jardine AG, Mark PB. Cardiovascular morbidity and mortality after kidney transplantation. *Transpl Int*. 2015;28:10–21.
8. Weir MR, Burgess ED, Cooper JE, et al. Assessment and management of hypertension in transplant patients. *J Am Soc Nephrol*. 2015;26:1248–1260.
9. Ponticelli C, Cucchiari D, Graziani G. Hypertension in kidney transplant recipients. *Transpl Int*. 2011;24:523–533.
10. Campistol JM, Romero R, Paul J, et al. Epidemiology of arterial hypertension in renal transplant patients: changes over the last decade. *Nephrol Dial Transplant*. 2004;19(Suppl_3):iii62–iii66.
11. Kasiske BL, Anjum S, Shah R, et al. Hypertension after kidney transplantation. *Am J Kidney Dis*. 2004;43:1071–1081.
12. Ojo AO. Cardiovascular complications after renal transplantation and their prevention. *Transplantation*. 2006;82:603–611.
13. Opelz G, Döhler B; Collaborative Transplant Study. Improved long-term outcomes after renal transplantation associated with blood pressure control. *Am J Transplant*. 2005;5:2725–2731.
14. Carpenter MA, John A, Weir MR, et al. BP, cardiovascular disease, and death in the Folic Acid for Vascular Outcome Reduction in Transplantation trial. *J Am Soc Nephrol*. 2014;25:1554–1562.
15. Aziz F, Clark D, Garg N, et al. Hypertension guidelines: how do they apply to kidney transplant recipients. *Transplant Rev (Orlando)*. 2018;32:225–233.
16. Midtvedt K, Hartmann A. Hypertension after kidney transplantation: are treatment guidelines emerging? *Nephrol Dial Transplant*. 2002;17:1166–1169.
17. Becker GJ, Wheeler DC, Zeeuw DD, et al. Kidney Disease: Improving Global Outcomes (KDIGO) Blood Pressure Work Group. KDIGO clinical practice guideline for the management of blood pressure in chronic kidney disease. *Kidney Int Suppl*. 2012;2:337–414.
18. Åsberg A, Skrunes R, Vikse BE, et al. *Norsk Nyreregister årsrapport for 2018 med plan for forbedringstiltak*. 2019. Available at https://www.kvalitetsregistre.no/sites/default/files/36_arsrapport_2018_norsk_nyreregister_0.pdf. Accessed January 11, 2020.
19. Dobrowolski LC, Bemelman FJ, van Donselaar-van der Pant KA, et al. Treatment efficacy of hypertension in kidney transplant recipients in the Netherlands. *Neth J Med*. 2014;72:258–263.
20. Ruzicka M, Quinn RR, McFarlane P, et al. Canadian Society of Nephrology commentary on the 2012 KDIGO clinical practice

guideline for the management of blood pressure in CKD. *Am J Kidney Dis*. 2014;63:869–887.
21. Williams B, Mancia G, Spiering W, et al; ESC Scientific Document Group. 2018 ESC/ESH guidelines for the management of arterial hypertension. *Eur Heart J*. 2018;39:3021–3104.
22. Calhoun DA, Jones D, Textor S, et al; American Heart Association Professional Education Committee. Resistant hypertension: diagnosis, evaluation, and treatment: a scientific statement from the American Heart Association Professional Education Committee of the Council for High Blood Pressure Research. *Circulation*. 2008;117:e510–e526.
23. Brook RD, Townsend RR. Treatment of resistant hypertension. In: Bakris GW, White WB, ed. *UpToDate*. 2020. Available at https://www.uptodate.com/contents/treatment-of-resistant-hypertension. Accessed September 28, 2020.
24. Opelz G, Wujciak T, Ritz E. Association of chronic kidney graft failure with recipient blood pressure. Collaborative Transplant Study. *Kidney Int*. 1998;53:217–222.
25. Gustavsen MT, Midtvedt K, Lønning K, et al. Evaluation of tools for annual capture of adherence to immunosuppressive medications after renal transplantation – a single-centre open prospective trial. *Transplant Int*. 2019;32:614–625.
26. Ho PM, Bryson CL, Rumsfeld JS. Medication adherence: its importance in cardiovascular outcomes. *Circulation*. 2009;119:3028–3035.
27. Bramley TJ, Gerbino PP, Nightengale BS, et al. Relationship of blood pressure control to adherence with antihypertensive monotherapy in 13 managed care organizations. *J Manag Care Pharm*. 2006;12:239–245.
28. Lee JK, Grace KA, Taylor AJ. Effect of a pharmacy care program on medication adherence and persistence, blood pressure, and low-density lipoprotein cholesterol: a randomized controlled trial. *JAMA*. 2006;296:2563–2571.
29. Nöhre M, Schieffer E, Hanke A, et al. Obesity after kidney transplantation-results of a KTx360°substudy. *Front Psychiatry*. 2020;11:399.
30. Mallamaci F, Tripepi R, D'Arrigo G, et al. Long-term blood pressure monitoring by office and 24-h ambulatory blood pressure in renal transplant patients: a longitudinal study. *Nephrol Dial Transplant*. 2019;34:1558–1564.