Hypertension after kidney transplantation
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CHAPTER 3

EPIDEMIOLOGY AND MANAGEMENT OF HYPERTENSION IN PAEDIATRIC AND YOUNG ADULT KIDNEY TRANSPLANT RECIPIENTS IN THE NETHERLANDS


* Both authors contributed equally

ABSTRACT

Introduction
Hypertension in kidney transplant recipients (KTRs) is a risk factor for cardiovascular mortality and graft loss. Data on the prevalence of hypertension and uncontrolled hypertension (uHT) in paediatric and young adult KTRs are scarce. Also, it is unknown whether ‘transition’ (the transfer from paediatric to adult care) influences control of hypertension. We assessed the prevalence of hypertension and uHT among Dutch paediatric and young adults KTRs and analysed the effects of transition. Additionally, we made an inventory of variations in treatment policies in Dutch transplant centres.

Methods
Cross-sectional and longitudinal national data from living KTRs ≤ 30 years (≥ 1 year post-transplant, eGFR > 20ml/min) were extracted from the ‘RICH Q’ database, which comprises information about all Dutch KTRs aged < 19 years, and the Netherlands Organ Transplant Registry database for adult KTRs (≥ 18-30 years). We used both upper limit blood pressure (BP) thresholds for treatment according to KDIGO guidelines. UHT was defined as a BP above the threshold. A questionnaire on treatment policies was sent to paediatric and adult nephrologists at 8 Dutch transplant centres.

Results
Hypertension and uHT were more prevalent in young adult KTRs (86.4% and 75.8%) than in paediatric KTRs (62.7% and 38.3%) according to the KDIGO definition. Time after transplantation was comparable between these groups. Longitudinal analysis showed no evidence of effect of transition on systolic BP or prevalence of uHT. Policies vary considerably between and within centres on definition of hypertension, BP measurement and antihypertensive treatment.

Conclusion
Average BP in KTRs increases continuously with age between 6 and 30 years. Young adult KTRs have significantly more uHT than paediatric KTRs according to KDIGO guidelines. Transition does not influence prevalence of uHT.
INTRODUCTION

Hypertension after kidney transplantation increases the risk of cardiovascular disease (CVD) and has disadvantageous effects on allograft function in adults as well as in children.1-6 Though outcomes such as CVD are not frequently manifested in paediatric patients, the risk for CVD at older age is established early in childhood. Long-term follow-up studies show that CVD accounts for over 40% of premature deaths in patients with paediatric onset of end-stage renal disease.7,8 Recent data demonstrates that improvement of cardio-protective management, especially antihypertensive treatment, lowers the risk for cardiovascular comorbidity and mortality. Uncontrolled hypertension, defined as persistent blood pressure (BP) measurement above the target value with or without being treated, is an established risk factor contributing to CVD and is therefore regarded as a potential target to ameliorate the prognosis of transplant patients.9,10 In kidney transplant recipients (KTRs), the reported prevalence of hypertension varies from 59% in children to up to 85% in older adults.1,11-15 However, these data are derived from large registry databases and mostly based on single BP measurements. To our knowledge, data on prevalence rates of hypertension and uncontrolled hypertension in paediatric KTRs are scarce and those of that for young adult KTRs (aged 18-30 years) are hardly available.

The variation in reported prevalence may be caused by a difference in definitions used for hypertension. For adult KTRs, the Kidney Disease Improving Global Outcome (KDIGO) guideline recommends maintaining BP below 130/80 mmHg.16 However, by the WHO guidelines, this level is regarded as the threshold for pre-hypertension and the WHO defines genuine hypertension as BP measurements of 140/90 mmHg and above, irrespective of treatment.16-18 For children, the National High Blood Pressure Education Program (NHBPEP) recommends the p95 upper limit for both systolic and diastolic BP as the threshold to define genuine hypertension and the p90 upper limit for so-called pre-hypertension that does not warrant medical treatment.19 In contrast, the KDIGO guideline recommends using the p90 upper limit as threshold for medical treatment of high BP in children with renal failure, based on evidence derived from the ‘Effect of Strict BP Control and angiotensin converting enzyme (ACE) Inhibition on the Progression of Chronic Renal Failure in Pediatric Patients’ (ESCAPE) study.17,20

Furthermore, the effect of ‘transition’ from paediatric to adult care around the age of 18 years is believed to be associated with a reduced adherence to medication regimens. Transition might therefore lead to a reduction in the control of hypertension.21-25 To what extent transition affects the prevalence of uncontrolled hypertension in young KTRs is unknown.

Earlier studies showed that different management policies among centres and countries affect outcome in children with chronic kidney disease.26-28 Policy variation in the post-transplant antihypertensive care has not been studied.
In this study we aimed to assess the prevalence and differences in prevalence of hypertension and uncontrolled hypertension (uHT) between paediatric and young adult KTRs using different BP thresholds for defining hypertension. Furthermore, we aimed to assess the effect of transition on BP and treatment of hypertension. Finally, we made an inventory differences in antihypertensive treatment policies among adult and paediatric nephrologists.

METHODS

For performing cross-sectional and longitudinal analyses, we extracted data from the ‘Renal Insufficiency Therapy in CHildren – Quality assessment and improvement project’ (RICH-Q) for the paediatric patients and data from the Netherlands Organ Transplant Registry (NOTR) for adult patients. Patients were stratified by age in 5 groups: children aged 4-6 years, 7-12 years, 13-17 years, and young adults aged 18-24 years and 25-30 years.

The RICH-Q project is a multicentre registry including all patients with ESRD aged < 19 years. Data have been prospectively collected from October 2007 onwards in all Dutch, Belgian and 3 German paediatric nephrology centres. For this study only Dutch data were used. The NOTR database is a nationwide registry containing anonymised data since 1968 of all patients who underwent organ transplantation. Both registries comprise longitudinal information on demographics, transplantation details, recipient and donor characteristics, body composition, BP and rejection episodes and medication. For cross-sectional and longitudinal analyses, we included KTRs with eGFR ≥ 20 ml/min and with a transplant vintage of ≥ 1 year, since stable BP control is often not achieved within the first year post-transplant. Data were retrieved on May 28th 2014, using the latest available visit registration of patients who were at the retrieval date. Since the NOTR database records plasma creatinine and not eGFR, we calculated eGFR using the Modification of Diet in Renal Disease (MDRD) equation as well as the Schwarz formula for adults to compare kidney function in children and adults. Missing values for heights in adults were imputed with the mean for > 18 year-old males (mean 175.2 cm) and females (mean 162.0 cm) to calculate eGFR using the Schwartz formula. Children with missing height values were excluded. Reference values of healthy age-matched children were used to define BP targets. BP for paediatric KTRs are expressed in percentiles based on general population values for age, sex and height.

For the effect of transition on BP and uHT, we acquired longitudinal data of individual KTRs with a transplant ≥ 1 year, eGFR ≥ 20 ml/min, and aged ≤ 30 years on May 28th 2014. All their available records were included. Data from both databases were merged using transplant identification numbers. From these records, we selected a cohort of patients who had a minimum of two BP recordings both before and after the transition moment, defined as the date on which the treating paediatric nephrologist had ended the registration in the RICH-Q registry.
Hypertension definitions

Table 1 provides an overview of the 2 different thresholds for ‘hypertension’. 1) A blood pressure above the defined threshold at which anti-hypertensive treatment is recommended, used in KTRs for both children and adults, i.e. the KDIGO guideline for BP management in patients with chronic renal disease and renal transplant recipients, version 2012. 2) The WHO (adult guidelines) and 4th Pediatric Task Force NHBPEP 2004 guideline on hypertension in the general population. The threshold according to the KDIGO guidelines is consistent with p90 values according to WHO/Task force.16-18,31-35

Firstly, we defined hypertension as BP above the recommended threshold and normal BP with anti-hypertensive treatment. This includes all patients except for normotensive patients without antihypertensive treatment. Also, we use the terms ‘controlled hypertension’ and ‘uncontrolled hypertension’. Systolic BP (SBP) and/or diastolic BP (DBP) persistently measured below target values while treated with one or more antihypertensive agents is defined as controlled hypertension. Uncontrolled hypertension (uHT) is a BP above the recommended threshold with or without therapy (uHT treated vs. uHT untreated). Normotension is defined as a BP below target values without treatment.

We inventoried treatment policies among 8 adult and 4 paediatric nephrology centres using an online questionnaire, which was developed in collaboration with paediatric and adult nephrologists to ensure content validity. The questionnaire included questions on local official (written) protocols for post-transplant hypertension treatment, on methods of BP measurement, frequency of screening for hypertension, BP registration, and definitions of hypertension, estimated prevalence rates and on preferences in antihypertensive drugs (Appendix). The physician in charge of every academic adult and
paediatric kidney transplant centre received the request to distribute the questionnaire among their transplant nephrologists.

**Statistical analysis**

Statistical analyses were performed using IBM SPSS Statistics 21.0 (IBM Corp, USA). Non-normally distributed data are presented as medians with interquartile ranges (IQR). $P$-values below 0.05 are considered statistically significant. Growth models were performed using Mplus 7.0 (Muthén&Huhtén, USA).\(^{36}\) to examine individual development over time. Two ‘piecewise growth models’ were used: 1) Individuals’ development of systolic BP (continuous variable), and 2) Individuals’ development of hypertension over time (dichotomous variable). We used the moment of transition as initial status or ‘intercept’. Two piecewise random slopes were calculated and compared: the first random slope represents the average ‘growth’ rate (i.e. increase in mmHg or uHT risk) per year until the moment of transition; and the second slope represents the average ‘growth’ rate per year from transition onwards.

**RESULTS**

Data from 640 paediatric and adult patients aged $\leq$ 30 years with a functioning graft were available on May 28\(^{th}\), 2014. One hundred and seventy-four subjects met the exclusion criteria: data from within first year after transplantation ($n=108$) more than one transplant ($n=4$); missing heights for children ($n=4$); missing creatinine data ($n=3$); eGFR $\leq$ 20 ml/min ($n=55$); leaving 466 patients for analysis. Patient characteristics are given in Table 2.

**Prevalence of hypertension and uncontrolled hypertension**

Figures 1 and 2 show the prevalence of hypertension and uHT. In Figure 2 the classification is divided into normotension (BP under target without treatment), hypertension with treatment (BP under target level with treatment) and treated and untreated uHT. Hypertension according to KDIGO was significantly more prevalent in young adult patients than in paediatric KTRs (86%, 95% CI 82-90% vs. 76%, 95% CI 67-82%; $p=0.007$). When the WHO/Task Force thresholds were used, the difference in hypertension between adult (72.0%, 95% CI 67-76%) and paediatric (70.0%, 95% CI 61-77%) KTRs was smaller and not significant ($p=0.681$).

UHT, according to KDIGO, was also more prevalent in young adult patients (63.0%, 95% CI 58-68%) as compared to paediatric KTRs (38.3%, 95% CI 30-47%, $p<0.0001$). The prevalence of uHT according to WHO/NHBPEP was also statistically different between children (7.5%, 95% CI 4-14%) and adults (24.0%, 95% CI 20-29%, $p<0.001$), but showed a U-shape curve when all age groups were compared, with the highest percentages in patients of 4-6 yrs (25.0%, 95%CI 10-50%) and 25-30 yrs (30.4%, 95%CI 24-38%) and the lowest in patients 13-17 yrs (1.6%, 95% CI 0-9%) ($p<0.001$ between groups). In 11 (23%) paediatric patients with uHT ($n=7$, aged 7-12 yrs, $n=4$, 12-17 yrs)
no antihypertensive agents were prescribed. In 87 (42%) adult patients (n=38, 22% aged 18-24 yrs, n=49, 20% aged 25-30 yrs) no antihypertensive drug was registered while having uHT. Table 3 demonstrates the BP and its regulation.

Figure 3 presents the mean systolic BP with 95% CI in the cross-sectional analysis, showing a higher BP in older patients.

Transition
Criteria for inclusion in the longitudinal analysis were met in 105 patients. Figure 4 presents the development of the average SBP in the 5 years before and 5 years after transition. The mean intercept at transition (t=0) was 124.5 mmHg (95% CI 122.4-126.6) for systolic BP. Before transition, the average change in systolic BP per year was not significantly different from zero with 0.11 mmHg (95% CI -0.50 - 0.72). After transition, SBP significantly decreased by 0.80 mmHg (95% CI -1.58 - 0.02) per year. There was no statistically significant effect of transition on the risk of uHT 5 years before and 5 years after transition. Before transition, the slope over the 5 year period, indicating the risk change was -0.1% (95% CI -7.9% - 7.7%) whereas in the 5 year period after transition, the risk of uHT increased but not significantly (2.6%, 95% CI -6.2% - 11.2%).

Policies
All 4 paediatric and 7 out of 8 adult centres and their member nephrologists responded to the questionnaire. Response rates were not assessed since the number of physicians receiving the questionnaire per centre was not known. Results are described in
Table 4a and 4b. Written official policies on antihypertensive treatment were available in 2/4 paediatric and in 6/7 adult centres.

BP measurements are performed at every visit in all centres. In paediatric departments, a nurse performs all BP measurements. While in the adult centres, BP is measured by
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In all paediatric centres and according to 16 adult nephrologists, BP is measured in sitting position. Three adult nephrologists measure BP in supine position.

The number and duration of BP measurements varies from one single measurement to 15 min continuous measurements.

The BP registered in the medical chart varies between listing ‘each individual measurement’ (7 adult, 2 paediatric nephrologist), the lower of 2 measurements (7 adult, 1 paediatric) or the mean of 2 or 3 measurements (3 adult, 1 paediatric nephrologist).

Two adult nephrologists reported not to know which BP is registered. Hypertension is defined by 11 adult nephrologists as BP > 130/80 mmHg, by 4 as > 130/90 mmHg, by 1 as > 135/85 mmHg and by 3 as > 140/90 mmHg. The BP threshold of p90 is used by 2 paediatric nephrologists, 2 use p95 as threshold.

Table 2. Patient characteristics

<table>
<thead>
<tr>
<th>Demographics</th>
<th>4-6 years</th>
<th>7-12 years</th>
<th>13-17 years</th>
<th>18-24 years</th>
<th>25-30 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (male), n (%)</td>
<td>14 (88)</td>
<td>24 (56)</td>
<td>34 (56)</td>
<td>103 (59)</td>
<td>100 (59)</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>5.5 ± 0.8</td>
<td>10.3 ± 1.8</td>
<td>16.3 ± 1.4</td>
<td>21.8 ± 22.1</td>
<td>27.6 ± 1.3</td>
</tr>
<tr>
<td>Ethnicity Caucasian</td>
<td>12 (75)</td>
<td>31 (72)</td>
<td>24 (65)</td>
<td>No data</td>
<td>No data</td>
</tr>
<tr>
<td>Weight SDS</td>
<td>-0.3 [-1.0-0.8]</td>
<td>-0.1 [-0.9-0.8]</td>
<td>-0.8 [-1.2-0.4]</td>
<td>-0.3 [-1.0-1.4]</td>
<td>0.6 [-0.4-1.3]</td>
</tr>
<tr>
<td>Height SDS</td>
<td>-0.9 [-1.6 - -0.2]</td>
<td>-1.1 [-1.8- -0.7]</td>
<td>-1.3 [-1.9- -0.6]</td>
<td>-1.4 [-2.4 - -0.4]</td>
<td>-0.9 [-1.7 - -0.1]</td>
</tr>
<tr>
<td>Body Mass index SDS</td>
<td>0.6 [0.1-1.1]</td>
<td>0.5 [0.1-1.5]</td>
<td>0.4 [-0.2-1.2]</td>
<td>1.0 [-0.2-2.0]</td>
<td>1.1 [0.2-1.9]</td>
</tr>
<tr>
<td>Age at Tx (yrs)</td>
<td>3.0 [2.0-3.8]</td>
<td>7.0 [5.0-8.0]</td>
<td>12.0 [9.5-14.0]</td>
<td>17.0 [13.0-19.0]</td>
<td>23.0 [19.0-25.0]</td>
</tr>
<tr>
<td>Time after Tx (yrs)</td>
<td>2.5 [2.0-3.0]</td>
<td>4.0 [3.0-5.0]</td>
<td>5.0 [3.0-10.0]</td>
<td>5.0 [3.0-11.0]</td>
<td>4.0 [2.0-9.0]</td>
</tr>
<tr>
<td>Donor type (living), n (%)</td>
<td>11 (69)</td>
<td>21 (49)</td>
<td>31 (51)</td>
<td>113 (65)</td>
<td>112 (66)</td>
</tr>
</tbody>
</table>

Graft function

| eGFR MDRD (ml/min) | - | - | - | 54 [39-65] | 49 [40-61] |
| Proteinuria (g/L) | 0.10 [0.06-0.31] | 0.10 [0.07-0.15] | 0.12 [0.09-0.22] | 0.15 [0.06-0.32] | 0.2 [0.09-0.50] |

Immunosuppression

| Mycophenolate | 12 (75) | 21 (49) | 36 (59) | 104 (62) | 97 (59) |
| Prednisolone (%) | 7 (44) | 31 (72) | 40 (66) | 134 (80) | 146 (79) |
| Tacrolimus (%) | 15 (94) | 38 (88) | 44 (72) | 103 (62) | 94 (55) |
| Azathioprine (%) | 1 (6) | 1 (2) | 4 (7) | 25 (15) | 27 (17) |
| Cyclosporine (%) | 1 (6) | 1 (2) | 10 (16) | 22 (13) | 12 (7) |
| mTOR (%) | 0 | 5 (12) | 4 (7) | 8 (5) | 13 (8) |

Values are presented as median (IQR) unless otherwise indicated. Unknown values: n=16, n=73 and n=170 for age groups 13–17 years, 18–24 years and 25–30 years, respectively. Abbreviations: Tx = transplantation; SDS = standard deviation score; mTOR = mammalian target of rapamycin. a Schwartz formula: when height was missing in adult KTRs, the mean height of 18-year-old KTRs was used; b Mycophenolate is either mycophenolate acid or mycophenolate mofetil; c Valid per cent: for 18–24 years, 8 missing values; for 25–30 years, 9 missing values. The percentage of the group of which the data were known is presented.
First choice antihypertensive agents by both adult and paediatric nephrologists were calcium antagonists and ACE-inhibitors. Although beta-blockers were not included in top three choices of antihypertensive agents in children, according to the registry in 26% of the KTRs aged 13-17 years beta-blockade was prescribed. Paediatric nephrologists estimated the prevalence of hypertension to be 40% [IQR 23-50%], adult nephrologists 70% [IQR 50-75%].

**DISCUSSION**

This is the first study that addresses prevalence rates of hypertension and uHT in paediatric as well as young adult KTRs and assesses the effect of transition. We show that the prevalence of hypertension and uHT in children and young adult KTRs in the age range of 4 to 30 years tends to be higher in the relatively older subjects, which is comparable with other literature. Uncontrolled HT, meaning untreated or undertreated hypertension, shows a high prevalence, especially among young adult
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KTRs. We also demonstrate the difference in hypertension prevalence using KDIGO and WHO/Task Force definitions. Transition from paediatric to adult nephrologic care did not show any influence on BP. We also demonstrate a wide variation in frequency and methods of BP measurements and official policies on antihypertensive treatment within and between centres and between paediatric and adult nephrologists.

In the general population, BP as well as the prevalence of hypertension increases with age. However, between 15 and 40 years, systolic BP remains stable in healthy subjects. In contrast to this, we found an increasing systolic BP in KTRs at a younger age (25-30 years). This suggests that apart from the physiological increase in systolic BP over time, an additional mechanism causes a BP increment in KTRs. This is probably due to hypertension-inducing factors such as arterial stiffness and immunosuppressive use, related to transplant and chronic kidney disease (CKD).

The difference in prevalence of hypertension among the age groups might be due to a difference in primary renal disease or the cumulative duration of renal replacement therapy rather than the differences in management policies. However, although these factors were not included in the analysis, the time after transplantation has been comparable and the linear association between age and increase of systolic BP suggests that the susceptibility to vascular stiffening in CKD patients increases with age.

In particular, the young adult KTRs were often undertreated according to both the KDIGO guidelines and, to a far lesser extent, the WHO guidelines. This under-treatment can partly be explained by the inconsistency in the official recommendations, which is also reflected in the variety in management policies that we found among physicians. Explicitly, KDIGO 2009 guidelines recommend thresholds for the treatment of high BPs at levels equal to so-called pre-hypertension in non-renal patients for adults as well as for children. The evidence for the downward adjustment to the p90 and 130/80 thresholds is based on

![Figure 3. Mean systolic blood pressure with 95% CI for kidney transplant recipients (cross sectional)](image-url)
observational studies and evidence from CKD non-dialysis (ND) dependent patients. As is stated in KDIGO 2009: “In KTRs, there is little reason to believe that the prevention and treatment of hypertension would not also prevent CVD and kidney allograft injury”. In the 2012 revision of KDIGO, however, the recommendation for CKD transplant children had disappeared, but the overall recommendation for BP management in CKD ND children - the same p90 recommendation - had been upgraded to level 1c, based on the ESCAPE studies. The confusion derives from the paucity of evidence on the beneficial effects of anti-hypertensive treatment on CVD and graft outcome. This applies to adults as well as children. As the majority of transplanted patients have a degree of CKD, there is a motive to apply non-dialysis dependent CKD guidelines for hypertension management to this group of patients. It emphasizes the need for long-term studies in paediatric and young adult KTRs to estimate the effect of BP on cardiovascular outcome. We could not find a negative effect of transition from paediatric to adult care on the prevalence of uncontrolled hypertension. Transition is a concern since it may lead to a presumed reduced adherence to the prescribed therapy as a result of a different, on average less directive, patient approach from adult nephrologists compared to paediatric nephrologists. Less therapy adherence might induce a higher prevalence of hypertension and periods of rejection.

Samuel et al. found an adjusted hazard ratio for graft loss within the adaptation period after transition compared with the period before transition of 2.24 (95%CI 1.19-4.20). However, the crude failure rate of 6.6 per 100 person-years of losing the graft within the adaptation period of 2.5 years after transition was only slightly higher than after the adaptation period (i.e. for young adults), in which the crude failure rate was 5.1 per 100 person-years. Watson et al. reported that 40% of young adults (age range 15.7 – 20.9 years) lost their renal graft within 36 months of transition. However, this retrospective

Figure 4. Observed and estimated means of SBP and time to transition; error bars indicate 95% CI.
study included only 20 patients of which the majority (5/7) of patients with a rejection had psychosocial difficulties identified prior to transplantation. Moreover, in 4/7 patients low immunosuppressive levels were found, which may be due to non-adherence, but may also be caused by insufficient dosages. Not all studies support these effects of transition: Van den Heuvel et al. showed no increased risk of rejection or graft failure after transition.46 Although we do not have data on therapy adherence, our data imply that there is no adverse effect from transition on BP control and therefore there is most likely no adverse effect on adherence to anti-hypertensive medication either.

**Policies**

In this study we also found differences in policies, definitions and management of hypertension after renal transplantation. Previous studies have also shown a considerable variation in management policies among centres for paediatric dialysis and transplantation.26-28,47 As shown in this study, paediatric and adult nephrologists have different management policies for post-transplant hypertension. We believe that this inconsistency in management of hypertension in the clinical practice is rooted in the absence of prospective studies from which clear guidelines can be formed for this specific patient group. It is likely that the policy variation contributed to the differences in prevalence of (uncontrolled) hypertension but we could not study this since both registries contain anonymised data and therefore we were unable to trace which patient is treated by which centre or physician. Adult nephrologists gave a better estimation of the ‘true’ prevalence than paediatric nephrologists. This may be due to a higher awareness and prevalence of vascular disease and hence of hypertension among adult KTRs. The exact indication for a prescribed drug was not registered. We were aware of the potential overestimation of antihypertensive agents since e.g. ACE inhibitors (ACEi) are more likely to be prescribed for other indications (e.g. proteinuria reduction) than for

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**Table 4a. Results of the questionnaire on post-transplant antihypertensive policies**

<table>
<thead>
<tr>
<th>Respondents</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Official policy</td>
<td>yes</td>
<td>no</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>Written policy</td>
<td>yes</td>
<td>unknown</td>
<td>yes</td>
<td>unknown</td>
</tr>
<tr>
<td>Policy base</td>
<td>D</td>
<td>CD</td>
<td>B</td>
<td>B</td>
</tr>
<tr>
<td>Screening frequency</td>
<td>every visit</td>
<td>every visit</td>
<td>every visit</td>
<td>every visit</td>
</tr>
<tr>
<td>Position</td>
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<td>sitting</td>
<td>sitting</td>
<td>sitting</td>
</tr>
<tr>
<td>Method BP measurement</td>
<td>automatic</td>
<td>automatic</td>
<td>automatic</td>
<td>manual</td>
</tr>
<tr>
<td>1st choice antihypertensive</td>
<td>calcium ant.</td>
<td>unknown</td>
<td>ACEi</td>
<td>calcium ant.</td>
</tr>
<tr>
<td>2nd choice antihypertensive</td>
<td>diuretic</td>
<td>unknown</td>
<td>ATII block</td>
<td>diuretic</td>
</tr>
<tr>
<td>3rd choice antihypertensive</td>
<td>alpha block</td>
<td>unknown</td>
<td>ACEi</td>
<td>calcium ant.</td>
</tr>
</tbody>
</table>

* Only four centres for paediatric nephrology have a paediatric kidney transplantation program.

* A = unknown; B = international guidelines; C = literature; D = expert opinion; E = national guidelines. Abbreviations: ACEi = angiotensin-converting enzyme inhibitor; AT II = angiotensin II receptor blocker; calcium ant = calcium antagonist.
heterogeneity. Calcium antagonists and ACEi were preferred for primary treatment, but there was considerable heterogeneity. These variations in preferred antihypertensive treatment are a consequence of the absence of recommendations for pharmacological treatment in present guidelines.

**Limitations**

This study has several limitations. Firstly, there were small numbers of patients available, especially in the youngest groups of 4-6 years and 7-13 years. However, this is currently the largest Dutch cohort available. The level of treatment success could not be assessed, since we were not informed about medication dosage or medication adherence. Due to the relatively small number of patients in the longitudinal analysis, the distribution

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**Table 4b. Results of the questionnaire on post-transplant antihypertensive policies**

<table>
<thead>
<tr>
<th>Adult centers</th>
<th>1</th>
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<th>4</th>
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<th>6</th>
<th>7</th>
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<tbody>
<tr>
<td>Respondents</td>
<td>5</td>
<td>2</td>
<td>5</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>1</td>
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<tr>
<td>Official policy</td>
<td>Yes</td>
<td>5</td>
<td>0</td>
<td>2</td>
<td>3</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Written policy</td>
<td>Yes</td>
<td>5</td>
<td>0</td>
<td>2</td>
<td>3</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Policy base</td>
<td>1xA, 1xB, 1xCD, 1xCD, 1xBC, 1xCD, 1xCD, 1xBE, 1xB, 1xBC, 1xCD, 1xB, 1xBC, 1xCD, 1xCD, 1xCD, 1xB, 1xBC</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Screening frequency</td>
<td>Every visit</td>
<td>3</td>
<td>2</td>
<td>3</td>
<td>3</td>
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<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Method BP measurement</td>
<td>Automatic</td>
<td>4</td>
<td>2</td>
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</tr>
<tr>
<td>1st choice antihypertensive</td>
<td>Calcium ant.</td>
<td>5</td>
<td>2</td>
<td>3</td>
<td>2</td>
<td>0</td>
<td>1</td>
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<tr>
<td>2nd choice antihypertensive</td>
<td>Calcium ant.</td>
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<tr>
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<tr>
<td>AT II block</td>
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<tr>
<td>Alpha block</td>
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</tr>
</tbody>
</table>

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*Abbreviations: ACEi = angiotensin-converting enzyme inhibitor; AT II = angiotensin II receptor blocker.*

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$a$ A = unknown; B = international guidelines; C = literature; D = expert opinion; E = national guidelines.

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of the average SBP in the 5 years before and 5 years after is large. Moreover, we
considered those patients receiving treatment with antihypertensive agents as having
hypertension. We were aware that some antihypertensive drugs are prescribed for
other medical symptoms or conditions than hypertension, such as ACEi for proteinuria.
Moreover, we noticed that 24 h BP measurements would give better indications of
true BP courses. However very few of these records are available in the registry since
they are not routinely performed in children nor in young adult KTRs.

Although we used all available follow-up data, we cannot rule out the possibility that a
proportion of less adherent patients is not included in the analysis. However, we know
that in both the paediatric nephrology care and adult nephrology care, adherence to
follow-up is up to 95%. We could not assess response rates on the questionnaire since
the head of each department distributed the questionnaires among the transplant
nephrologists and the number of informed physicians remains unknown. Moreover,
we used data in which we could not verify the accuracy and differences in methods
and in registration accuracy between physicians and between centres. Finally, in the
questionnaire we did not discriminate between differing times after transplantation
(we included patients from one year after transplant and beyond). This may influence
results, as patients with hypertension shortly after transition, are treated different
compared to those with a longer follow up after transplantation.

CONCLUSION

Hypertension and uncontrolled hypertension after kidney transplantation is more
common in subjects between 25 and 30 years than in younger subjects. The transfer
from paediatric to adult care does not influence BP or hypertension prevalence. Policies
regarding BP targets and methods of BP measurements vary among the treating
physicians, both within and between groups of adult and paediatric nephrologists.
Close attention to BP regulation is needed, especially in young adult KTRs.

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