

## CHAPTER 8.7 Arterial hypertension

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### Introduction

Arterial hypertension is a common complication in children after kidney transplantation (prevalence 60–90%) and is an important risk factor for graft failure and increased cardiovascular morbidity and mortality in children. Therapeutic control of hypertension is often inadequate; 50–80% of treated transplanted children have persistent hypertension and isolated nocturnal hypertension is a common finding.

### Diagnosis

Ambulatory 24-hour blood pressure monitoring (ABPM) is the method of choice to diagnose hypertension and blood pressure rhythm disturbances in transplanted children. It should be performed once a year in all transplanted children and 3–6 months after any change in antihypertensive therapy. Regular clinical follow-up should always include standardised office blood pressure measurement (ESH Guidelines 2016) at each outpatient visit. In addition, home blood pressure measurements are recommended and should be encouraged. Regular checks for hypertension-mediated organ damage (HMOD) should be carried out including echocardiography (once a year), albuminuria/proteinuria (once a month) and fundoscopy (especially in high-risk patients, to be included in the annual check by an ophthalmologist).

## Antihypertensive medication

No controlled trials have been conducted on the treatment of hypertension in transplanted children. In transplanted adults, the antihypertensive effects of different classes of antihypertensive drugs are comparable, with ACE inhibitors/angiotensin receptor blockers also having antiproteinuric effects.

All five basic classes of antihypertensive drugs can be prescribed (calcium channel blockers, diuretics, beta-blockers, ACE inhibitors, angiotensin receptor blockers). Some antihypertensive drugs approved for the use in children are listed in table 1. The choice of drugs is empirical, but in certain conditions and comorbidities the use of specific antihypertensive drugs may be beneficial (e.g. ACE inhibitors/angiotensin receptor blockers for concomitant proteinuria or left ventricular hypertrophy, or diuretics for volume or salt overload). Combination antihypertensive therapy is often required to achieve adequate blood pressure control. In severe, refractory hypertension, use of additional antihypertensive drug classes (e.g., mineralocorticoid receptor antagonists (MRA),  $\alpha_1$ -blockers, centrally acting agents or vasodilators) may be required.

**Contraindications:** Same as for antihypertensive therapy in non-transplanted children (e.g., ACE inhibitors/angiotensin receptor blockers in renal graft artery stenosis). It should be kept in mind that graft function in transplanted children may be more sensitive to dehydration events than in children with native kidney CKD. In girls with child-bearing potential RAAS blockers can be prescribed, but contraceptive measures are mandatory.

**Goal of therapy:** The target blood pressure for transplanted children and adults is not known and the recommended limits are based on expert consensus (EBM level C). The office blood pressure target should be at least < 95th percentile for both systolic and diastolic blood pressure. For ABPM, the target blood pressure should be < 95th percentile for both day and night. There is currently no data on whether a target blood pressure of < 90th percentile or even lower (as recommended for children with native kidney CKD) is more beneficial for transplanted children.

**Table 1** Antihypertensive medications with clinical experience in children

Antihypertensive drug class	Generic name	Recommended daily dose	Divided in
ACE-inhibitors	Captopril*	Up to 6 mg/kg/day	3 doses
	Enalapril	up to 0.6 mg/kg/day	2 doses
	Ramipril*	1.5 to 6 mg/m <sup>2</sup> /day	1 dose
	Lisinopril*	0.08–0.6 mg/kg/day (max.40mg/day)	1 dose
Angiotensin-receptor blockers	Losartan	0.7 to 1.4 mg/kg/day	1 dose
	Irbesartan	6–12 years: 75 to 150 mg/day ≥ 13 years: 150 to 300 mg/day	1 dose
	Candesartan	0.15–0.5 mg/kg	1 dose
Beta-Blockers	Propranolol	0.5 to 6 mg/kg/day	2–3 doses
	Atenolol	1 to 2 mg/kg/day	1–2 doses
	Metoprolol	0.5 to 2 mg/kg/day	1–2 doses
Calcium channel blockers	Nifedipine SR, GITS*	0.5 to 3 mg/kg/day	3–4 doses
	Amlodipine*	0.6 to 0.15 mg/kg/day	1 dose
	Felodipine	0.5 to 1 mg/kg/day	1 dose
	Isradipine	0.5 to 1 mg/kg/day	1 dose
Diuretics	Hydrochlorothiazide	0.5 to 3 mg/kg/day	2 doses
	Furosemide	1 to 3 mg/kg/day	2–3 doses

Although every effort has been made to confirm the recommended doses by consulting appropriate references, manufacturers' prescribing information is frequently updated and should be consulted.

\*Antihypertensive drugs for which clinical experience in kidney transplanted children exists based on published studies

## References

- 1 Arbeiter K, Pichler A, Stemberger R, Mueller T, Ruffingshofer D, Vargha R, Balzar E, Aufricht C (2004) ACE inhibition in the treatment of children after renal transplantation. *Pediatr Nephrol* 19:222–226
- 2 Lurbe E, Agabiti-Rosei E, Cruickshank JK, Dominiczak A, Erdine S, Hirth A, Invitti C, Litwin M, Mancina G, Pall D, Rascher W, Redon J, Schaefer F, Seeman T, Sinha M, Stabouli S, Webb NJ, Wühl E, Zanchetti A. 2016 European Society of Hypertension guidelines for the management of high blood pressure in children and adolescents. *J Hypertens*. 2016 Oct;34(10):1887–920.
- 3 Opelz G, Wujciak T, Ritz E for the Collaborative Transplant Study (1998) Association of chronic kidney graft failure with recipient blood pressure. *Kidney Int* 53:217–222
- 4 Opelz G, Dohler B, Collaborative Transplant Study (2005) Improved long-term outcomes after renal transplantation associated with blood pressure control. *Am J Transplant* 5:2725–2731
- 5 Seeman T, Vondrák K, Dušek Effects of the strict control of blood pressure in pediatric renal transplant recipients – ESCORT trial. *J. Pediatr Transplant*. 2019 Feb;23(1):e13329.
- 6 Seeman T, Feber J. Should ACE inhibitors or calcium channel blockers be used for post-transplant hypertension? *Pediatr Nephrol*. 2021 Mar;36(3):539–549.
- 7 Seeman T, Myette RL, Feber J (2023): Hypertension in pediatric kidney transplantation. *Pediatr Transplant*. 2023 Aug;27(5):e14522.
- 8 Sugianto RI, Grabitz C, Bayazit A, Duzova A, Thurn-Valsassina D, Memaran N, Doyon A, Canpolat N, Kaplan Bulut I, Azukaitis K, Obrycki Ł, Anarat A, Büscher R, Caliskan S, Harambat J, Lugani F, Ozcakar ZB, Paripović D, Ranchin B, Querfeld U, Schaefer F, Schmidt BMW, Melk A. Stricter Blood Pressure Control Is Associated With Lower Left Ventricular Mass in Children After Kidney Transplantation: A Longitudinal Analysis of the 4C-T Study. *Hypertension*. 2023 Sep;80(9):1900–1908.
- 9 Sugianto RI, Schmidt BMW, Memaran N, Duzova A, Topaloglu R, Seeman T, König S, Dello Strologo L, Murer L, Özçakar ZB, Bald M, Sheenoy M, Buescher A, Hoyer PF, Pohl M, Billing H, Oh J, Staude H, Pohl M, Genc G, Klaus G, Alparslan C, Grenda R, Rubik J, Krupka K, Tönshoff B, Wühl E, Melk A. Sex and age as determinants for high blood pressure in pe-

- diatric renal transplant recipients: a longitudinal analysis of the CERTAIN Registry. *Pediatr Nephrol.* 2020 Mar;35(3):415–426.
- 10 Tian Z, Bergmann K, Kaufeld J, Schmidt-Ott K, Melk A, Schmidt BMW. Left Ventricular Hypertrophy After Renal Transplantation: Systematic Review and Meta-analysis. *Transplant Direct.* 2024 May 17;10(6):e1647.