Polish Society of Hypertension

2015 Guidelines for the Management of Hypertension

Part 9

Recommendations of the Polish Society of Hypertension

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Arterial Hypertens. 2015, vol. 19, no. 3, pages: 101–119
DOI: 10.5603/AH.2015.0014

9. Hypertension in children and adolescents

Data from randomized studies and representative population studies indicate that hypertension is present in 3–5% of children and adolescents aged 0–18 years, and its incidence increases with age. In the OLAF and OLA studies, conducted in representative population samples, BP values above the 95th percentile for age and gender, calculated as the mean of the second and third BP measurement during a single visit, were noted in 6.9% of children aged 3 years, 7.7% of children aged 6–10 years, and 6.2% of youths aged 10–20 years. In Polish studies studies (3 measurements during 3 independent visits), hypertension was found in about 10% large-city adolescents aged 18 years, which is consistent with the rate of hypertension among young adults aged 20–30 years. Secondary hypertension is the major cause of hypertension in younger children. With increasing rates of obesity in children and adolescents, the proportion of primary hypertension increases and it is diagnosed in about 50% of all children evaluated due to hypertension.

The following recommendations regarding the management of hypertension in children and adolescents have been developed based on the previously published fourth report of the National High Blood Pressure Education Program Working Group on Children and Adolescents, paediatric guidelines of the ESH, ESC, the American Heart Association (AHA), and the American Academy of Paediatrics (AAP), specific guidelines of other societies, literature review, and expert opinion.

9.1. Recommendations regarding screening for hypertension

According to the ESH guidelines and the fourth report of the National High Blood Pressure Education Program Working Group on Children and Adolescents, BP should be measured in children above 3 years of age at least once a year during routine health supervision visits and visits related to health problems. In children below 3 years of age, BP measurement is recommended in selected cases in children with identified health problems (Table XXVII). In Poland, according to the ordinance of the Minister of Health, BP should be measured in each child above 12 months of age during each physician consultation. This recommendation is not supported by society guidelines and epidemiological study findings. BP measurements in younger children are at a high risk of failure due to lack of patient cooperation: the proportion of unreliable BP measurements is 41% in children at one year of age, 20% in children aged 3 years, and 9% of children aged 3–6 years.

9.2. Diagnosis of hypertension

9.2.1. Definitions and classification of hypertension in children and adolescents

According the generally accepted definition of hypertension in children, this diagnosis requires BP readings ≥ 95th percentile for age, gender, and height during three independent visits. Classification of hypertension in children and adolescents depends on the method of BP measurement. Based on office measurements (using the auscultatory or oscillometric method), the following categories are distinguished:

Normal BP — BP values below the 90th percentile for age, gender, and height;

- **High normal BP (Europe) or prehypertension (United States)** — SBP and/or DBP between the 90th and 95th percentile, and BP > 120/80 mm Hg in adolescents;
- **Hypertension** — mean SBP and/or DBP values ≥ 95th percentile for age, gender, and height in at least three independent measurements;
- **White coat hypertension** — office BP measurements above the 95th percentile but home BP or ABPM values within normal limits;
- **Grade 1 hypertension** — BP values between the 95th percentile and 5 mm Hg above the 99th percentile for age, gender, and height;
- **Grade 2 hypertension** — BP values more than 5 mm Hg above the 99th percentile for age, gender, and height.

In the classification of hypertension in children that was adopted in both European and U.S. guidelines, categories of severe hypertension and hypertensive urgencies and emergencies have not been defined. However, the following definitions of these conditions are used for practical reasons:

- **Severe hypertension** — BP values more than 30 mm Hg above the 99th percentile for age, gender, and height;
- **Hypertensive urgencies** — impending organ failure related to hypertension, requiring rapid intervention, usually with concomitant unspecific symptoms such as headache and vomiting;
- **Hypertensive emergencies** — established or acute organ damage related to hypertension, mostly with organ failure, symptoms of encephalopathy, and Keith-Wagener-Barker grade 3 and/or grade 4 retinopathy on fundoscopy.

Table XXVII. Blood pressure measurements in children and adolescents — indications and technique.

BP should be measured in all children aged > 3 years at least once a year and during any routine physician examination.
Technique and indications:
• BP measurement is more reliable if the child has not eaten a meal within 30 minutes before the measurement, has not received medications that might affect BP, and has been resting in a sitting position with its back supported in a quiet environment for 5–10 minutes before the measurement.
• During the initial consultation, BP should be measured on all four limbs. During the first year of life and until the child assumes the upright position, BP readings in the lower limbs are lower than in the upper limbs. During the second year of life in a child who stands/walks, BP readings in the lower limbs are higher by about 20 mm Hg, and at a later age they are higher by about 30–40 mm Hg.
• Subsequent measurements should be performed on the right arm that is fully exposed, abducted and supported at the level of the heart.
• The cuff should encircle the full circumference of the arm and cover at least two thirds of its length. The inflatable bladder should encircle at least 80% of the arm circumference, including the whole medial aspect of the arm. A measurement performed using a cuff that is too narrow may overestimate BP by as much as 30%, and underestimate BP if the cuff is too wide.
• In infants, the body position has no significant effect on BP values. During sleep, SBP values in infants are lower by 5–7 mm Hg.
• As readings obtained during the first measurement are usually overestimated, in such cases — BP should be measured 2–3 times on one occasion.
• BP readings above the 90th percentile by the oscillometric method require verification by the auscultatory method.
• If the BP difference between the upper limbs is ≥ 5 mm Hg, this fact should be noted in the medical record.
In younger children (< 3 years), BP should be measured in the following situations:
• perinatal morbidity (prematurity, low birth weight, perinatal intensive therapy)
• congenital anomalies
• recurrent urinary tract infections, other renal and/or urinary tract disease
• cancer
• solid organ or bone marrow transplantation
• use of drugs affecting BP
• symptoms and conditions associated with hypertension (neurofibromatosis, tuberous sclerosis, others), intracranial pressure rise

BP, blood pressure

The classification of hypertension based on ABPM also includes the category of masked hypertension, defined as abnormal BP values in ABPM and normal BP values in office measurements (Table XXVIII).

9.3. Reference blood pressure values

9.3.1. Reference values for office measurements

It is recommended to use reference BP values for a given age, gender and height developed for specific BP measurement methods (auscultatory, oscillometric). For BP measurements using the auscultatory method, the most commonly used are reference values for children aged 0–18 years, developed for the population of the United States, Canada, Mexico, and Great Britain and published in the fourth report of the National High Blood Pressure Education Program Working Group on Children and Adolescents. For oscillometric (automated) BP measurements,

Table XXVIII. Blood pressure classification in children based on ambulatory blood pressure monitoring (based on Flynn *et al.*, Hypertension 2014)

Category	Office BP	Mean SBP and/or DBP by ABPM	SBP and/or DBP load
Normal BP	< 90th percentile	< 95th percentile	< 25%
White coat hypertension	≥ 95th percentile	< 95th percentile	< 25%
Masked hypertension	< 95th percentile	≥ 95th percentile	< 25%
High normal BP	≥ 90th percentile and/or 120/80	< 95th percentile	25–50%
Ambulatory hypertension	≥ 95th percentile	≥ 95th percentile	25–50%
Severe ambulatory hypertension	≥ 95th percentile	≥ 95th percentile	> 50%

ABPM, ambulatory blood pressure monitoring; BP, blood pressure; DBP, diastolic blood pressure; SBP, systolic blood pressure

reference values developed for the Polish population of children aged 3–18 years (www.olaf.czd.pl) are recommended.

9.3.2. Home blood pressure measurements

In children with the diagnosis of hypertension, home BP measurements using a validated oscillometric device are recommended. Use of the reference values developed by Stergiou *et al.* for children and adolescents aged 6–18 years is recommended (Table XXIX). No reference BP values were developed for HBPM in younger children. Evaluation based on BP measurements twice daily during at least 3 days is considered reliable, and the optimal approach involves morning and evening BP measurements performed during 7 subsequent days. Adequate home BP measurements are considered a reliable indicator of the effectiveness of antihypertensive therapy.

9.3.3. Ambulatory blood pressure measurement

Ambulatory BP measurement using a validated oscillometric device is recommended in all children above 5 years of age in whom hypertension was diagnosed based on office BP measurements. Use of the reference BP values for ABPM developed by Wühl *et al.* and adopted in the 2014 AHA guidelines is recommended. Routine repeated ABPM is recommended to evaluate treatment effects.

9.3.4. Interpretation issues

When interpreting BP measurements, age, gender, and height of the patient should be taken into consideration. Significant issues have been raised for neonates (see "Neonatal hypertension" below), children in the first year of life, and adolescents, as well as interpretation of oscillometric measurements including ABPM. In neonates and children in the first year of life in whom BP was measured, evaluation of SBP only is recommended. Of note, the 95th percentile SBP values for girls aged 13–18 years are much lower compared to those for boys, and at the age of 18 years, the 95th percentile values for both SBP and DBP in girls are 5–10 mm Hg lower than 140/90 mm Hg. The latter values correspond to 99th percentile in girls aged 18 years.

As most currently used ABPM devices are based on the oscillometric method, it should be emphasized that with this method, the mean arterial pressure (MAP) is directly evaluated, and SBP and DBP values are calculated using appropriate algorithms. In addition, results of some controlled paediatric studies (e.g., the ESCAPE study) and therapeutic recommendations (see below) are based on the analysis of MAP values. Another interpretation issue related to ABPM is the fact that using this method, higher BP values comparted to office measurements are obtained in children below 10 years of age and those with the height below 120 cm. Due to lacking reference values and the above mentioned interpretation issues, routine use of ABPM is not recommended in children below 5 years of age.

Table XXIX. Reference home blood pressure values (95th percentile) in boys and girls (based on Stergiou *et al.*, Am. J. Hypertens. 2008)

Height	Girls	Boys
120–129	119/74	119/76
130–139	120/76	121/77
140–149	122/77	125/77
150–159	123/77	126/78
160–169	124/78	128/78
170–179	125/79	132/78
180–189	128/80	134/79

9.4. Methods to evaluate target organ damage

Basic approaches to evaluate the severity of hypertensive target organ damage in children include:

- evaluation of left ventricular mass, systolic function, and diastolic function by echocardiography;
- ECG;
- fundoscopy;
- evaluation of renal function.

9.4.1. Evaluation of left ventricular mass

Left ventricular mass (LVM) is a major criterion of target organ damage in hypertension. Echocardiography is the standard method to diagnose left ventricular hypertrophy, and ECG is only an additional diagnostic tool due to its low specificity and the need for age-specific interpretation. The most commonly used approach to evaluate LVM is based on the recommendations of the American Society of Echocardiography and uses the Deveraux formula. As LVM depends on height, it is recommended to calculate LVM indexed for height in meters to the power of 2.7 according to the formula suggested by DeSimone. Published reference values and percentiles of the LVM index calculated using this formula allow using this parameter in children over 1 year of age. A limitation of indexing LVM for height is the possibility to overdiagnose left ventricular hypertrophy in obese children in comparison to indexing for fat-free body weight. Nevertheless, it is currently the most commonly used and recom-

mended approach to evaluate LVM in children and adolescents that allows not only comparisons of echocardiographic findings in children of varying age but also comparing paediatric data with the results obtained in adults. The principles of evaluating left ventricular systolic and diastolic function are the same as in adults.

Definitions:

— left ventricular hypertrophy — LVM ≥ 95th percentile for age and gender (Table XXX)
— severe ventricular hypertrophy — LVM index ≥ 51 g/m$^{2.7}$*

9.4.2. Fundoscopy

The principles of fundoscopic examination in children do not differ from those in adults. The Keith-Wagener-Barker classification is commonly used in clinical practice. A simplified classification includes 2 types of changes, benign and malignant. Benign changes are Keith-Wagener-Barker grade 1 and/or grade 2 lesions, and malignant changes are grade 3 and/or grade 4 lesions. The simplified classification allows initial patient selection for more or less intensive treatment.

9.4.3. Evaluation of renal damage

Routine methods to evaluate renal function include glomerular filtration rate (GFR) estimation using the Schwartz formula and/or serum cystatine C level measurements. Albuminuria is an indicator of hyperfiltration and/or microvascular damage. There are no commonly accepted reference values for albuminuria in children, and adult cut-off values are used in practice, with albuminuria above 30 mg/24 h corresponding to the 95th percentile values.

Hyperuricaemia is considered an abnormality specific for hypertension. However, it is not clear whether an increased uric acid level is a primary phenomenon or occurs secondarily to subclinical renal damage.

9.4.4. Non-obligatory additional tests to evaluate the extent of target organ damage in children and adolescents

Non-obligatory additional tests to evaluate the extent of target organ damage in children and adolescents include:

- evaluation of large artery damage (measurement of the intima-media thickness [IMT]);
- measurement of the pulse wave velocity (PWV).

During the last decade, multiple reports have been published that support using IMT and PWV measurements to evaluate target organ damage, and reference IMT and PWV values for children and adolescents aged 6–20 years have been reported (Tables XXXI and XXXII).

Table XXX. Reference left ventricular mass index values (95th percentile) in children (based on Khoury *et al.*, J. Am. Soc. Echocardiogr. 2009)

Age	95th percentile LVMI [g/m$^{2.7}$]	
	Boys	Girls
< 6 months	80.1	85.6
≥ 6 months to ≤ 2 years	68.6	57.1
2 years to ≤ 4 years	52.4	55.3
4 years to ≤ 6 years	48.1	44.3
6 years to ≤ 8 years	44.6	43.5
8 years to ≤ 10 years	41	36
10 years to ≤ 12 years	38.2	35.7
12 years to ≤ 14 years	41.4	38.2
14 years to ≤ 16 years	40.5	36.9
≤ 16 years	39.4	40

LVMI, left ventricular mass index

Table XXXI. Reference common carotid artery intima-media thickness values (50th and 95th percentile) in millimetres (based on Doyon *et al.*, Hypertension 2013) (values rounded to the nearest 0.01 mm; reprinted with permission from Standardy Medyczne)

	50th percentile		95th percentile	
Age (years)	Boys	Girls	Boys	Girls
6	0.37	0.36	0.44	0.43
7	0.37	0.37	0.44	0.43
8	0.37	0.37	0.44	0.44
9	0.37	0.37	0.45	0.44
10	0.38	0.37	0.45	0.44
11	0.38	0.38	0.45	0.44
12	0.38	0.38	0.46	0.44
13	0.38	0.38	0.46	0.45
14	0.39	0.38	0.47	0.46
15	0.39	0.38	0.47	0.46
16	0.4	0.39	0.48	0.46
17	0.4	0.39	0.48	0.46
18	0.40	0.39	0.48	0.47

*In observational studies in adults, LVM index ≥ 51 g/m$^{2.7}$ (approximately corresponding to the 99th percentile of LVM in the paediatric population) has been associated with a 4-fold increase in the risk of a cardiovascular event over 5 years

Table XXXII. Reference pulse wave velocity values (95th and 97th percentile) evaluated by tonometry (PulsePen; based on Reusz *et al.*, Hypertension 2010) and the oscillometric method (Vicorder; based on Fischer *et al.*, J Hypertens 2012; reprinted with permission from Standardy Medyczne)

Age (years)	PulsePen (tonometry)		Vicorder (oscillometric method)	
	Boys (95th percentile, m/s)	Girls (95th percentile, m/s)	Boys (97th percentile, m/s)	Girls (97th percentile, m/s)
7	5.4	5.2	4.8	4.8
8	5.5	5.4	5.0	5.0
9	5.5	5.5	5.1	5.1
10	5.6	5.6	5.2	5.3
11	5.8	5.8	5.4	5.4
12	5.9	5.9	5.5	5.5
13	6.1	6.0	5.7	5.6
14	6.3	6.0	5.8	5.7
15	6.5	6.2	6.0	5.7
16	6.7	6.3	6.2	5.7
17	6.9	6.5	6.3	5.6
18	7.1	6.7		
19	7.3	6.9		

9.5. Principles of the differential diagnosis of hypertension in children and adolescents

Differential diagnosis of hypertension in children includes three steps (Table XXXIII). The extent of diagnostic investigations depends on the severity of hypertension, patient's age, and concomitant conditions. Indications for more extensive investigations that include diagnostic steps 1 and 2 are younger patient's age (before puberty; an arbitrarily chosen age threshold is 12 years) and/or grade 2 hypertension and/or presence of target organ damage and concomitant chronic conditions. Diagnostic step 1 includes confirmation of the diagnosis of hypertension, exclusion of white coat hypertension, grading the severity of hypertension, evaluation of target organ damage, and basic laboratory tests to exclude secondary hypertension. Diagnostic step 2 includes tests that require hospital admission and is generally appropriate in children with grade 2 hypertension and younger children with hypertension. Diagnostic step 3 includes highly specialized tests reserved for patients in whom the diagnosis has not been established despite completed step 1 and 2 investigations or hypertension is resistant to treatment.

The diagnosis of hypertension in children and adolescents should by confirmed by ABPM. Due to lacking reference values for younger children and the possibility of false positive diagnoses, only children above 5 years of age and/or above 120 cm in height should be routinely referred for ABPM. In younger children, the diagnosis of hypertension is based on office measurements.

In most children with hypertension, an immediate institution of antihypertensive therapy is not necessary, which usually allows complete diagnostic investigations before the treatment is started. Indications for initiating antihypertensive therapy before completion of the differential diagnosis include high BP values (grade 2 hypertension with clinical symptoms) and/or advanced target organ damage and/or symptomatic hypertension (hypertensive urgencies and emergencies). Except for hypertensive urgencies and emergencies, if drug treatment is necessary before completion of the diagnostic tests, long-acting dihydropyridine calcium antagonists are preferred as this drug class has the least effect on laboratory test findings.

9.6. General approach to the treatment of hypertension

General approach to and indications for the treatment of hypertension in children and adolescents are based on evaluation of the severity of hypertension, its nature (primary versus secondary), and concomitant conditions and target organ damage. Treatment monitoring and modifications based on ABPM are recommended (Figure 13). Antihypertensive drug treatment and its success rates depend on the aetiology of hypertension.

Table XXXIII. Diagnostic steps in children with hypertension (reprinted with permission from Standardy Medyczne 2008)

	Investigations	Comments
Step 1	• complete blood count, creatinine, sodium, potassium, chloride, calcium, bicarbonate, total cholesterol, triglycerides, HDL and LDL cholesterol, uric acid, glucose • urinalysis • daily albumin excretion or albumin/creatinine ratio in a spot urine sample • fundoscopy • kidney and renal artery Doppler ultrasound • ECG • echocardiography with evaluation of LVM and the aortic arch	Step 1 investigations should be performed in all patients with the diagnosis of hypertension
	• IMT measurement • transfontanellar ultrasound in neonates	IMT measurement is optional
	• ABPM in children > 5 years	ABPM is currently widely available; evaluation in children < 6 years has not been validated
Step 2	• glycaemia, oral glucose tolerance test, insulinaemia in patients with BMI >85th percentile	Oral glucose tolerance test is recommended as mandatory in patients with BMI > 85th percentile Fasting insulin allows calculation of HOMA-IR, and insulin in the fasting conditions and at 120 minutes after glucose administration allows evaluation of the insulin sensitivity index Multiple measurements during a 240-minute test allow calculation of areas under the glucose and insulin curves and are optional
	• urinary catecholamines in younger children and all patients with grade 2 hypertension • plasma renin activity/renin level and aldosterone level in younger children and all patients with grade 2 hypertension	
	• urinary steroid profile or urinary 17-keto- and 17-hydroxysteroids in younger children and all patients with grade 2 hypertension	Urinary steroid profile is currently recommended over previously used urinary 17-keto- and 17-hydroxysteroids
	• thyroid hormones, vitamin D3 metabolites	Measurements of thyroid hormones and vitamin D3 metabolites in patients with a suspicion of specific pathologies
	• renal scintigraphy (captopril test) in younger children and all patients with grade 2 hypertension	Dynamic scintigraphy is recommended to evaluate renal perfusion, urine excretion, relative renal function, and to estimate scarring (static DMSA scintigraphy is more sensitive in detecting scarring but does not allow evaluation of renal perfusion)
Step 3	• non-invasive and invasive renal artery imaging (CTA, MRA, invasive angiography) • imaging to detect adrenal lesions/paraganglioma • non-invasive imaging of other vascular beds (visceral arteries, intracranial arteries) • molecular testing	Step 3 investigations are performed in patients in whom the diagnosis has not been established despite completed step 1 and 2 investigations and/or treatment is unsuccessful

ABPM, ambulatory blood pressure monitoring; BMI, body mass index; CTA, computed tomography angiography; DMSA, dimercaptosuccinic acid; ECG, electrocardiogram; HDL, high-density lipoprotein; HOMA-IR, homeostatic model assessment-insulin resistance; IMT, intima-media thickness; LDL, low-density lipoprotein; LVM, left ventricular mass; MRA, magnetic resonance angiography

9.6.1. Primary hypertension

Primary hypertension is the major cause of hypertension in children above 12 years of age, accounting for about 50% of all cases of hypertension in the developmental period. The predominant intermediate phenotype of primary hypertension is abnormal body composition with visceral obesity, abnormal muscle-to-adipose tissue proportion, and metabolic disturbances typical for metabolic syndrome (Table XXXIV). The risk of target organ damage is related to the degree of metabolic abnormalities and the amount of visceral fat as evaluated by waist circumference.

9.6.1.1. Management of primary hypertension

Non-drug therapy including both dietary modifications and physical activity is of major importance in the management of primary hypertension. Dietary modifications are based on the principles of healthy eating and require limiting, and in practice essentially eliminating adding salt to foods and simple sugar consumption. Obese children with hypertension require a dietitian consultation and management as in simple obesity.

Exercise is of major importance in both prevention of essential hypertension and non-drug treatment of children with essential hypertension. Prospective

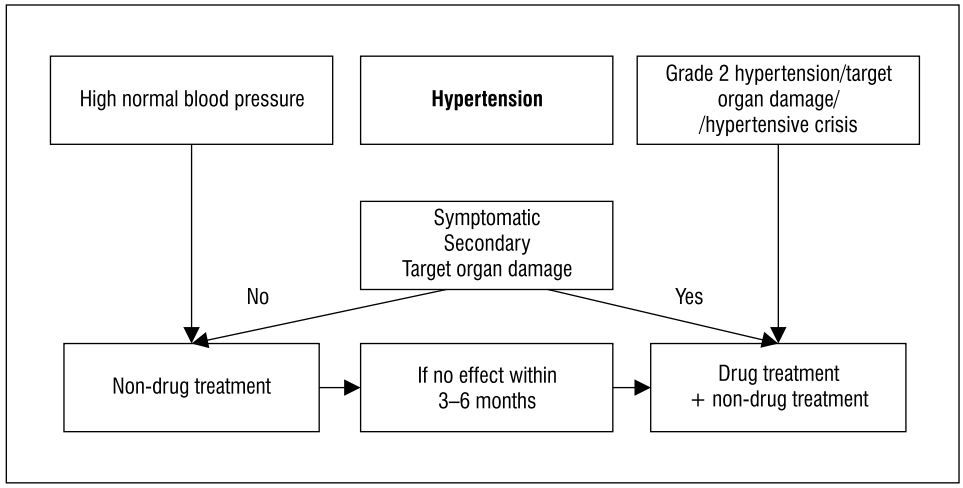

Figure 13. Treatment of hypertension in adolescents (modifications based on European Society of Hypertension, J. Hypertens. 2009; reprinted with permission from Standardy Medyczne)

Tabela XXXIV. Definitions of metabolic syndrome (based on Zimmet *et al*., Paediatric Diabetes 2007)

Age	Criteria
< 10 years	Metabolic syndrome should not be diagnosed. Extended diagnostic investigations are indicated in risk groups.
10–15 years (< 16 years)	Waist circumference ≥ 90th percentile or ≥ cut-off point for adult patients + 2 or more from the following criteria: — serum triglycerides ≥ 150 mg/dL — serum HDL cholesterol < 40 mg/dL — SBP ≥130 mm Hg and/or DBP ≥ 85 mm Hg — fasting blood glucose ≥ 100 mg/dL or type 2 diabetes
> 16 years	Criteria as in adults: — waist circumference ≥ 94 cm in boys and ≥ 80 cm in girls — serum triglycerides ≥ 150 mg/dL — serum HDL cholesterol < 40 mg/dL in boys and < 50 mg/dL in girls — SBP ≥ 130 mm Hg and/or DBP ≥ 85 mm Hg or antihypertensive drug treatment — fasting blood glucose ≥ 100 mg/dL or type 2 diabetes

DBP, diastolic blood pressure; HDL, high-density lipoprotein; SBP, systolic blood pressure

studies showed a beneficial effect of moderate-intensity regular exercise on BP lowering, increased flow-mediated endothelium-dependent vessel dilatation, and reduction of arterial stiffness in obese children. Daily high- to moderate-intensity exercise for 60 to 90 minutes is recommended.

9.6.1.2. Participation in sports by children and adolescents with essential hypertension

Major temporary contraindications to participation in sports include grade 2 hypertension until BP is controlled, and/or identification of severe target organ damage. Of note, however, no data indicate that even intensive dynamic exercise is associated with a significant risk. Similarly, no data indicate an association of static (isometric) exercise with an increased risk of complications. However, due to a significant increase in DBP, experts and societies (e.g., AAP) do not recommend class IIIA-C exercise (class IIIA — moderate physical activity: gymnastics, martial arts, sailing, rock-climbing, water skiing, weightlifting, windsurfing; class IIIB — moderately intense physical activity: body-building, alpine skiing, skateboarding, snowboarding, wrestling; class IIIC — intense physical activity: boxing, canoeing/rowing, cycling, triathlon and other multisport competitions) until BP is controlled in patients with grade 2 hypertension. Participation in sports is not contraindicated in patients with grade 1 hypertension.

Non-drug therapy as the major approach to the treatment of grade 1 hypertension is used for 3–12 months. Drug therapy should be considered in children with grade 1 hypertension in whom BP was not adequately lowered despite 6–12 months of non-drug therapy. Drug therapy is indicated in children with grade 2 hypertension and/or target organ damage. Due to concomitant metabolic disturbances, beta-blockers and diuretics are not recommended as

first- and second-line drugs, and the preferred drug classes are ACEI, ARB, and dihydropyridine calcium antagonists. In post-pubertal women who do not use contraception, new generation beta-blockers with vasodilatatory properties may be used, as these drugs do not induce adverse metabolic effects. Due to the fact that the risk of target organ damage is associated with metabolic disturbances and visceral obesity, it is recommended to include regular anthropometric measurements (waist circumference) in addition to evaluation of BP values and target organ damage when monitoring treatment effects.

9.7. Hypertension in chronic kidney disease

In the paediatric population, hypertension secondary to chronic kidney disease is the major cause of hypertension in younger children, and the major cause of severe hypertension with target organ damage at all ages. Hypertension is present in more than 54% of children with chronic kidney disease. Poorly controlled hypertension is a cause of cardiovascular deaths during renal replacement therapy. In addition, hypertension is a major risk factor for progression of chronic kidney disease. Goals of hypertension treatment in children with chronic kidney disease include both reduction of the risk of future cardiovascular events and delaying progression of chronic kidney disease. According to the ESC and Kidney Disease Improving Global Outcomes (KDIGO) guidelines, the BP threshold for initiating antihypertensive therapy is the 90th percentile for gender and age. Target BP values depend on the severity of proteinuria. These recommendations were based on the result of the ESCAPE study that showed that in children with proteinuria, the risk of chronic kidney disease progression is reduced by 35% with intensification of antihypertensive therapy compared to the conventional BP target. It is recommended to monitor antihypertensive treatment by ABPM, and treatment effectiveness should be evaluated bases on the mean 24-hour MAP. Reduction of the mean 24-hour MAP below the 90th percentile is recommended in children with chronic kidney disease without proteinuria or with proteinuria below 0.5 g per day, and below the 50% percentile in children with proteinuria above 0.5 g per day.

First-line antihypertensive drug classes in children with chronic kidney disease are RAAS inhibitors: ACEI and ARB. This is based on the pathomechanism of hypertension in chronic kidney disease and the published results of clinical trials and observational studies in children. Prospective multicentre studies showed the efficacy and safety of ACEI as antihypertensive and renoprotective drugs (ramipril, enalapril), and similar data were obtained for ARB (losartan) in single-centre studies. In addition, observational studies showed better BP control in children treated with RAAS inhibitors compared to other antihypertensive drug classes. These drugs are not recommended in patients with a very low GFR (< 15–20 mL/min/1.73 m^2) due to a risk of significant renal function worsening and/or hyperkalaemia. Dual therapy with ACEI and ARB may result in an additional BP-lowering effect and a reduction of proteinuria. However, such treatment is currently not recommended if additional indications are not present (antiproteinuric effect) due to concerns regarding the safety of such combined treatment. Renin inhibitors were tested in clinical studies in children but their renoprotective effect was not evaluated and these drugs continue not to be licensed for use in children.

Achieving target BP in patients with chronic kidney disease usually requires multiple antihypertensive drugs. Individualization of further drug treatment depending on the clinical scenario is recommended in children. Beta-blockers are the recommended second-line drugs in children with chronic kidney disease due to their additional effect on the RAAS and a reduction of proteinuria. Diuretics are recommended for fluid retention which is usually seen in children with GFR below 40 mL/min/1.73 m^2. In children with large proteinuria or low GFR, often the diuretic dose has to be increased for an adequate therapeutic effect. Thiazide/thiazide-like diuretics retain their effectiveness only in patients with GFR above 30–40 mL/min/1.73 m^2. Dihydropyridine calcium antagonists, previously used as first-line drugs in children with chronic kidney disease, are currently used as further choice drugs due to the fact that they increase proteinuria. This negative effect is absent or reduced in combination with RAAS inhibitors.

9.8. Renovascular hypertension

Renovascular hypertension is among the major causes of severe hypertension in children and adolescents. The main cause of renovascular hypertension in this age group is FMD, but in 20–40% of cases renovascular hypertension is a complication of other conditions (syndromic renovascular hypertension), including neurofibromatosis type 1 (>15%). Renovascular hypertension may also be caused by a congenital or acquired (e.g., transplant renal artery stenosis) stenosis of the main renal artery or additional renal arteries and/or segmental branches.

9.8.1. Investigations for and the diagnosis of renovascular hypertension

The diagnosis of renovascular hypertension is based on a finding of a hemodynamically significant stenosis of one or both renal arteries (Figure 14). Invasive angiography, often with selective renal artery catheterization, continues to be a reference method but should be performed only if percutaneous treatment is planned based on the results of non-invasive imaging. Routine evaluation of renal vein renin activity or level is not recommended. This test may be performed in case of diagnostic uncertainties.

9.8.2. Treatment of renovascular hypertension

The ultimate and causative therapy of renovascular hypertension is an interventional treatment that eliminates the underlying cause of hypertension. Although drug treatment allows at least partial BP control, it does not cure the patient. In patients with Takayasu disease, immunosuppressive treatment should be considered causative therapy.

9.8.2.1. Drug treatment of renovascular hypertension

The approach to drug treatment depends on whether unilateral or bilateral RAS is present (Table XXXV).

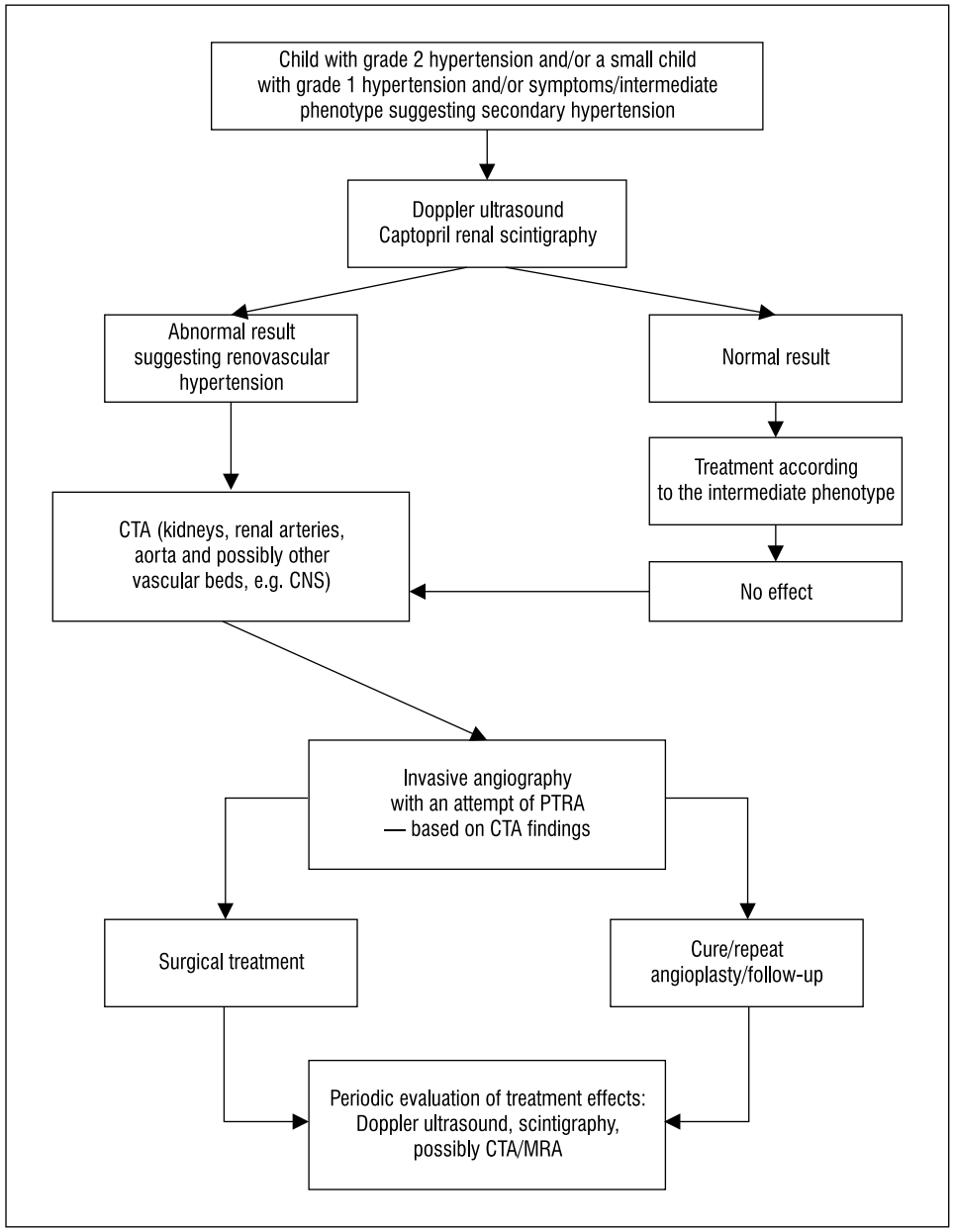

Figure 14. Diagnosis and treatment in children with renovascular hypertension

CNS, central nervous system; CTA, computed tomography angiography; MRA, magnetic resonance angiography; PTRA, percutaneous transluminal renal angioplasty

Table XXXV. Drug treatment of renovascular hypertension

Unilateral renal artery stenosis	Bilateral renal artery stenosis
ACEI/ARB	Diuretics
Dihydropyridine calcium antagonists	Dihydropyridine calcium antagonists
Beta-blockers	Beta-blockers
Alpha-blockers	Alpha-blockers
Centrally acting imidazoline agonists	Centrally acting imidazoline agonists

ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers

9.8.2.2. Interventional treatment of renovascular hypertension

Interventional treatment of renovascular hypertension includes percutaneous transluminal renal angioplasty (PTRA) and surgical revascularization. PTRA may be successfully undertaken by balloon angioplasty with or without stenting. PTRA is the initial step of the interventional treatment and it should it be attempted during invasive renal angiography. Complications of PTRA include mechanical vessel wall damage with formation of a pseudoaneurysm, thrombosis, arterial spasm, arterial wall laceration with bleeding, and entrapment of a balloon catheter within the vessel lumen. Some complications may require immediate surgical treatment, and thus both invasive renal angiography and PTRA should be performed in experienced paediatric centres with vascular surgical team backup. Local administration of an arterial smooth muscle relaxant should be always possible throughout the PTRA procedure. Drugs administered locally to relieve arterial spasm during PTRA include nifedipine, nitroglycerin, and sodium nitroprusside. According to experts' recommendations, prophylactic doses of low-molecular-weight heparin should be given for 1–7 days after the procedure in all cases of renal artery catheterization with PTRA, followed by administration of ASA at 1 mg/kg/day for 3–6 months.

Experience with stenting in renovascular hypertension in children and adolescents is relatively limited. Due to ongoing growth, stents mounted on balloon catheters that can be redilated later are recommended. If it is possible to implant a stent with a diameter corresponding to the size of the renal artery in an adult person, a self-expanding stent can be used.

9.8.2.3. Surgical treatment of renovascular hypertension

Two major approaches to the surgical treatment of renovascular hypertension are revascularization and nephrectomy. Surgical revascularization is indicated if drug therapy and PTRA were unsuccessful, and nephrectomy is indicated for unilateral RAS with severely impaired function of the ischemic kidney. Nephrectomy is considered appropriate if the ischemic kidney is reduced in size and its relative function has decreased to below 10–15%. In children and adolescents in whom renovascular hypertension is associated with an involvement of visceral vessels and/ /or midaortic syndrome, the therapeutic approach must be planned individually and mostly commonly involves staged procedures, taking into consideration their possible extent, type and sequence, including renal revascularization.

Major surgical techniques used for renal revascularization in adolescents include repair using a prosthetic or autologous patch, and kidney autotransplantation following excision of the stenosed arterial segment.

9.9. Hypertension in children after surgical treatment of coarctation of the aorta

Hypertension is an invariable and major symptom of congenital coarctation of the aorta. Following interventional treatment that resulted in a correction of the anatomical stenosis, hypertension persists or develops after a period of normotension in about 32.5% (25–68%) of patients. In a large proportion of patient, exercise-induced hypertension may be diagnosed based on an exercise test.

9.9.1. Treatment of hypertension in children after surgical treatment of coarctation of the aorta

Paediatric studies showed efficacy of ACEI (ramipril), ARB (candesartan), and metoprolol. AHA recommends ARB or ACEI and beta-blockers as first-line drugs. Routine annual ABPM and an exercise test every 2 years are recommended by the experts. Abnormal results of these tests are an indication for drug therapy and possible diagnostic investigations for recoarctation. According to the 2010 ESC guidelines, aortic imaging by MRI is recommended every two years in young adults who were treated for coarctation of the aorta.

9.10. Hypertension in children with type 1 diabetes

Hypertension is present in 5–25% of children with type 1 diabetes, and high normal BP is present

Table XXXVI. Treatment of hypertension in children with diabetes type 1

Threshold values	Treatment
BP > 90th percentile for age, gender, and height	Lifestyle changes*
BP > 90th percentile for age, gender, and height despite lifestyle changes	+ ACEI/ARB
BP > 95th percentile for age, gender, and heightLifestyle changes*	+ ACEI/ARB

*Body weight reduction to normal values (body mass index < 85th percentile) and physical activity >1 hour per day
ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; BP, blood pressure

in 30–40% of these children. Hypertension is much more prevalent in children with type 2 diabetes (30––50%). Diabetic patients are also characterized by an abnormal BP pattern, including non-dipping and rapid and significant morning BP surge.

Elevated BP is associated with significantly worse outcomes in patients with diabetes, as it is an important risk factor for micro- and macrovascular complications and premature mortality in this population. An abnormal BP pattern precedes development of diabetic nephropathy.

9.10.1. Indications for and approach to screening

According to AHA and AAP statements, BP measurement during each visit in a diabetic clinic in all children above 7 years (minimum 3 times a year) is recommended. In younger children, BP should be measured at least twice a year.

Investigations for secondary hypertension using the approach discussed above should be performed in patients with grade 2 hypertension, particularly if it is found during the first years after the diagnosis of diabetes and in all diabetic children below 10 years of age.

9.10.2. Treatment

The target BP is below the 90th percentile for age, gender, and height, and below 130/80 mm Hg in adolescents. Non-drug therapy including increased physical activity and dietary modifications is the basic approach to treatment. For drug therapy, the recommended antihypertensive drug classes are ACEI or, in case of ACEI intolerance, ARB. Drug treatment should be monitored by HBPM and ABPM, and the nocturnal BP fall should be taken into consideration (Table XXXVI).

9.11. Monogenic hypertension

The diagnosis of monogenic hypertension is based on the finding of a typical intermediate phenotype, which is often possible already during step 1 and 2 investigations. In some cases, a family history of hypertension associated with a typical phenotype or resistant to treatment may be ascertained (Figure 15). Autosomal dominant brachydactyly with hypertension has not been included in the presented scheme due to an unspecific biochemical phenotype (normal or mildly elevated plasma renin activity, normal aldosterone level) and a characteristic clinical phenotype. The diagnosis of a specific form of secondary hypertension allows successful treatment directed at its underlying cause.

9.12. Neonatal hypertension

Despite multiple data on normal BP values in neonates depending on specific measurement techniques, the definition of hypertension is still based on the percentile values reported in the 1987 Report of the Second Task Force on Blood Pressure Control in Children and derived from BP measurements using a mercury sphygmomanometer (Table XXXVII). According to the 1987 Report of the Second Task Force, hypertension may be diagnosed in neonates when SBP values above the 95th percentile for chronological age are found on three occasions. Table XXXVIII shows a compilation of previous reference BP values by Dionne at al. that summarizes the 95th and 99th SBP, DBP, and MAP percentiles in 2-week-old neonates born between 26 and 44 weeks of gestation. Despite numerous methodological limitations and the fact that BP is currently nearly always measured by the oscillometric method, reference BP values given in the 1987 Report of the Second Task Force are practical and easily obtainable.

Due to high rates of unreliable findings, including false positive results (up to 41% in children below 12 months of age), and resulting exposure to unnecessary investigations and treatment, BP measurement in healthy neonates is not recommended. Indications for BP measurement and investigations for hypertension are summarized in Table XXVII. It is recommended to perform BP measurements in appropriate conditions and using the technique described in Table XXXIX.

The incidence of hypertension in neonates is 0.2––0.3%, but it is much higher among premature infants and in selected risk groups. Hypertension was found in 0.81% of newborns hospitalized in neonatal intensive

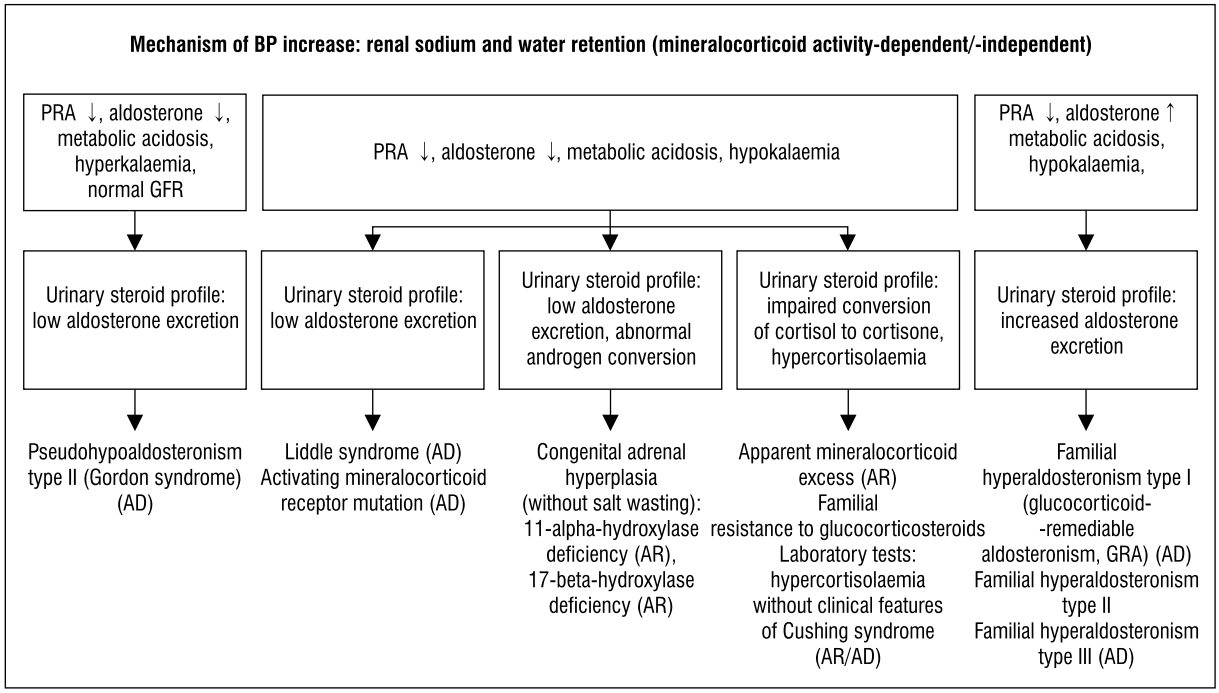

Figure 15. Diagnosis of monogenic hypertension based on the evaluation of the intermediate phenotype. Autosomal dominant brachydactyly with hypertension has not been included in the presented scheme due to an unspecific biochemical phenotype (normal or mildly elevated plasma renin activity, normal aldosterone level) and a characteristic clinical phenotype (reprinted with permission from Standardy Medyczne)
AD, autosomal dominant; AR, autosomal recessive; PRA, plasma renin activity

Table XXXVII. Reference systolic blood pressure values (95th percentile) in neonates (based on the 1987 Report of the Second Task Force; reprinted with permission from Standardy Medyczne)

Age	Reference SBP values during the first year of life — 95th percentile [mm Hg]	
	Boys	Girls
≤ 7 days	96	96
8–30 days	104	104
1 month	104	104
2 months	109	106
3 months	110	108
4 months	110	109
5 months	110	112
6–12 months	110	113

care units, but this rate increased to nearly 9% with the presence of additional risk factors (umbilical vessel catheterization, patent ductus arteriosus, intraventricular haemorrhage) and 40% in neonates with chronic bronchopulmonary disease. Neonatal hypertension is generally of a secondary nature, related mainly to renal pathology, most commonly renovascular disease, but iatrogenic factors are also of major importance.

The approach to the differential diagnosis of hypertension in neonates does not differ from that in older age groups. Investigations should be targeted at identification of hypertensive arteriolopathy, encephalopathy, left ventricular hypertrophy, and kidney damage. These investigations are also useful when evaluating the effectiveness of antihypertensive therapy (Table XL).

9.12.1. Treatment of neonatal hypertension

Given the lack of long-term randomized studies to evaluate outcomes of antihypertensive therapy in neonates, most recommendations are expert opinions based on clinical experience. It is not recommended to initiate treatment in asymptomatic neonates with BP values between the 95th and 99th percentile. Initiation of drug treatment is justified when BP values are above the 99th percentile, or target organ damage is present with BP values above the 95th percentile. The general rule of drug treatment in newborns and infants is to choose medications depending on the potential aetiology of hypertension and the presence of concomitant abnormalities, and the treatment should be started with as low doses as possible. The safest approach is to use short-acting intravenous drugs (Table XLI). Oral antihypertensive therapy is reserved for neonates in a good overall clinical condition (Table XLII).

Table XXXVIII. Blood pressure values at 2 weeks of life in neonates born between 26 and 44 weeks of gestation (based on Dionne *et al.*, Pediatr Nephrol 2012)

Postconceptional age	95th percentile	99th percentile
44 weeks of gestations		
SBP	105	110
DBP	68	73
MAP	**80**	**85**
42 weeks of gestation		
SBP	98	102
DBP	65	70
MAP	**76**	**81**
40 weeks of gestation		
SBP	95	100
DBP	65	70
MAP	**75**	**80**
38 weeks of gestation		
SBP	92	97
DBP	65	70
MAP	**74**	**79**
36 weeks of gestation		
SBP	87	92
DBP	65	70
MAP	**72**	**71**
34 weeks of gestation		
SBP	85	90
DBP	55	60
MAP	**65**	**70**
32 weeks of gestation		
SBP	83	88
DBP	55	60
MAP	**62**	**69**
30 weeks of gestation		
SBP	80	85
DBP	55	60
MAP	**65**	**68**
28 weeks of gestation		
SBP	75	80
DBP	50	54
b	**58**	**63**
26 weeks of gestation		
SBP	72	77
DBP	50	56
MAP	**57**	**63**

DBP, diastolic blood pressure; MAP, mean arterial pressure; SBP, systolic blood pressure

Table XXXIX. Technique of blood pressure measurements in neonates (based on Nwankwo *et al.*, Pediatrics 1997)

- Measurement using an oscillometric device
- 1.5 hours after feeding or a medical intervention
- Child supine or prone
- Selection of an appropriately sized cuff
- BP measurement on the right arm
- Earlier placement of the cuff and BP measurement after 15 minutes of a quiet rest
- BP measurement during sleep or in a quiet awake state
- 3 properly performed BP measurements 2 minutes apart

BP, blood pressure

Table XL. Criteria for the diagnosis of target organ damage in neonates (reprinted with permission from Standardy Medyczne)

Target organ damage	Diagnostic criteria
Eye fundus	Grade 3/4 retinopathy
Albuminuria	No reference values
Carotid artery IMT	No reference values, technically difficult to evaluate
• Features of hypertensive cardiomyopathy and aortopathy • Systolic dysfunction without left ventricular enlargement • Left ventricular hypertrophy • • Indirect evidence of left ventricular diastolic dysfunction — left atrial enlargement • Enlargement of the ascending aorta	• ejection fraction < 60% • shortening fraction < 29% • • • left ventricular mass index > 47.4 ± 6.2 g/m^2 • left atrial dimension > 1.89 ± 0.27 cm • • ascending aortic dimension > 1.04 ± 2 cm

9.13. Hypertensive urgencies and emergencies

Hypertensive emergency is defined as severe hypertension associated with acute target organ damage and/or failure, most commonly involving the central nervous system, heart and/or kidneys, and usually presenting with Keith-Wagener-Barker grade 3/4 retinopathy. Hypertensive urgency is defined as severe symptomatic hypertension without evidence of acute target organ damage and/or failure and without Keith-Wagener-Barker grade 3/4 retinopathy. In the developmental period, hypertensive emergencies are virtually always caused by secondary hypertension, including due to acute kidney disease (acute glomerulonephritis, haemolytic-uremic syndrome). Hypertensive urgencies associated with acute BP increases are also seen in children with primary hypertension. The management of hypertensive urgencies and emergencies has been evaluated in case reports and case series but not in controlled clinical studies,

Table XLI. Intravenous antihypertensive drugs used in neonates (reprinted with permission from Standardy Medyczne)

Antihypertensive drugs	Dosage	Mode of administration	Comments
Enalaprilat*	15 ± 5 μg/kg/dose, repeat q 8–24 hours	Injections every 5–10 minutes	May result in long-term hypotension or acute kidney failure Use limited due to these adverse effects
Esmolol	100–300 μg/kg/min	Intravenous infusion	Short-acting drug, continuous infusion necessary
Hydralazine*	Infusion: 0.75–5.0 μg/kg/min Bolus: 0.15–0.6 μg/kg/dose	Intravenous infusion or bolus	Frequent tachycardia; boluses given every 4 hours
Labetalol*	0.2–1.0 μg/kg/dose 0.25–3.0 μg/kg/hour	Intravenous bolus or infusion	Contraindications: heart failure, bronchopulmonary dysplasia
Nicardipine	1–3 μg/kg/min	Intravenous infusion	May result in reflex tachycardia
Sodium nitroprusside	0.15–10 μg/kg/min	Intravenous infusion	Risk of cyanide poisoning if long-term use or renal failure

*not available in Poland; may be obtained by a special physician prescription

Table XLII. Oral antihypertensive drugs used in neonates (reprinted with permission from Standardy Medyczne)

Antihypertensive drugs	Dosage	Mode of administration	Comments
Captopril	< 6 months: 0.01–0.5 mg/kg/dose Maximum 6 mg/kg/day	3 × day	Drug of choice in most neonates Need to monitor potassium and creatinine level
Clonidine	0.05–0.1 mg/kg/dose	2–3 × day	Causes dry mouth and somnolence Rebound hypertension if stopped abruptly
Hydralazine*	0.25–1.0 mg/kg/dose Maximum 7.5 mg/kg/day	3–4 × day	Tachycardia and fluid retention are frequent adverse effects
Isradipine	0.05–0.15 mg/kg/dose Maximum 0.8 mg/kg/day	4 × day	Effective in acute and chronic hypertension
Amlodipine	0.1–0.3 mg/kg/dose Maximum 0.6 mg/kg/day	2 × day	Hypotension less frequent than with isradipine
Propranolol	0.5–1.0 mg/kg/dose	3 × day	Maximum dose depends on heart rate: if bradycardia is not present, the dose may be increased to 8–10 mg/kg/day Contraindicated in bronchopulmonary dysplasia
Labetalol*	1.0 mg/kg/dose Maximum 10 mg/kg/day	2–3 × day	Contraindicated in bronchopulmonary dysplasia Need to monitor heart rate
Spironolactone	0.5–1.5 mg/kg/dose	2 × day	Results in potassium retention — need to monitor electrolytes Full effect seen after several days
Hydrochlorothiazide	1–3 mg/kg/dose	4 × day	Need to monitor electrolytes

*not available in Poland; may be obtained by a special physician prescription

and recommendations presented in the guidelines (2009 ESH guidelines and the 2004 fourth report of the National High Blood Pressure Education Program Working Group on Children and Adolescents) are based on expert opinion. It is recommended to treat hypertensive emergencies in an intensive care unit, with intravenous line access and ECG, BP, respiratory function (pulse oximetry), and fluid balance monitoring. Blood pressure should be measured every 15 minutes until it is reduced by 30% of the overall target BP reduction. In addition to fundoscopy, biochemical blood testing including renal function, electrolytes, and venous blood gases is recommended in all patients with hypertensive urgencies and emergencies, and if the aetiology of hypertension is not known, an initial differential diagnosis should also be performed including renal ultrasound with Doppler evaluation of the renal arteries and echocardiography to evaluate LVM. During subsequent hours of treatment, BP may be measured every 30––60 minutes depending on the clinical condition of the patient. The general approach to the treatment of a hypertensive emergency in children and adolescents is based on gradual, controlled BP reduction. It is recommended to lower BP by 25–30% of the overall target BP reduction within 6–8 hours and by another

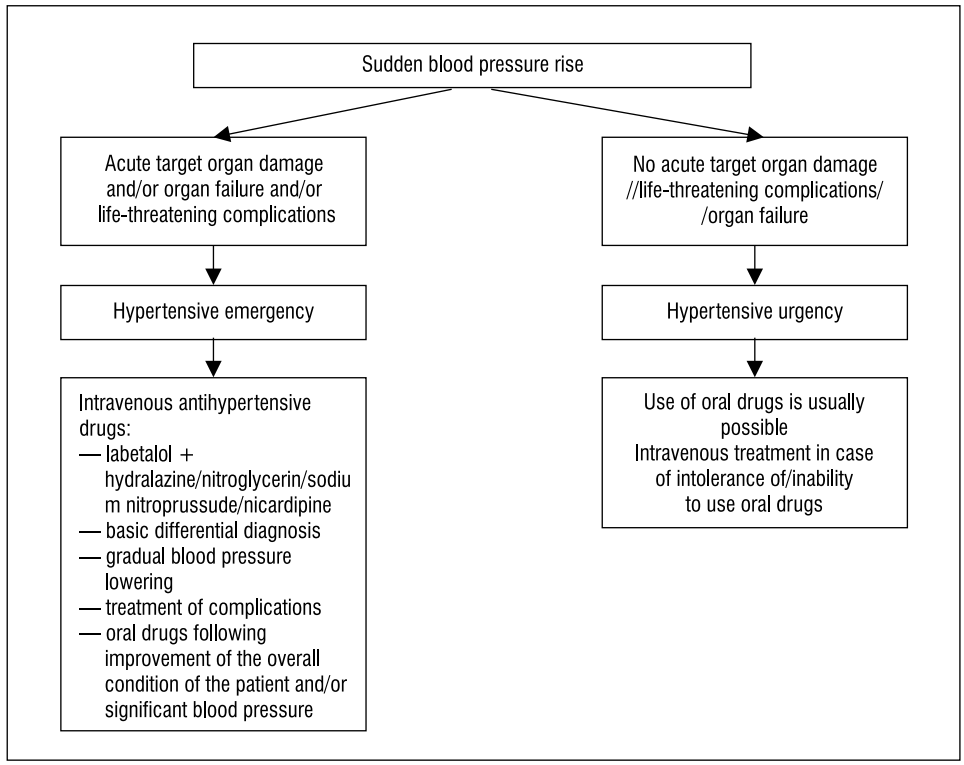

Figure 16. Management of hypertensive urgencies and emergencies. Reprinted with permission from Standardy Medyczne

30% within the next 24–36 hours. Normal BP values (< 90th to 95th percentile) should be reached within 72–96 hours. Intravenous medications are used for the treatment of hypertensive emergencies, with the choice of the drug based on the aetiology of hypertension. In hypertensive emergencies, administration of an intravenous beta-blocker (labetalol, esmolol) and a peripheral vasodilating agent (hydralazine, sodium nitroprusside, or nitroglycerin) is recommended. Due to fluid retention caused by peripheral vasodilation during prolonged therapy, an addition of a diuretic is also recommended. Oral treatment is initiated upon improvement of the general clinical condition of the patient. In hypertensive crises due to acute or chronic kidney disease (patients on dialysis therapy), volume control and removal of excess fluid by dialysis, or using diuretics in patients with preserved glomerular filtration, is of major importance. Addition of a RAAS inhibitor is recommended in hypertensive emergencies due to microangiopathy.

In hypertensive urgencies, oral treatment is usually possible. BP should lowered by 30% of the overall target BP reduction within the first 6 hours, and target BP values should be gradually reached during the next 36–48 hours. The management approach is shown in Figure 16, and dosage of the drugs used in hypertensive emergencies, along with their adverse effects and contraindications, is summarized in Table XLIII. In children with hypertensive urgencies and acute BP rises who may be treated with oral medications, rapidly acting drugs are recommended, followed by the institution of long-term antihypertensive therapy (Table XLIV).

Drug dosage for long-term antihypertensive therapy in children is summarized in Table XLV.

Table XLIII. Antihypertensive drugs used in hypertensive emergencies (reprinted with permission from Standardy Medyczne)

Antihypertensive drugs	Dosage	Mode of administration	Comments
Nicardipine*	Bolus: 30 μg/kg up to a maximum dose of 2 mg Infusion: 0.5–4 μg/kg/min	Intravenous bolus or infusion	May induce reflex tachycardia
Labetalol*	Bolus: 0.2–1 μg/kg up to a maximum dose of 40 mg Infusion: 0.25–3 μg/kg/hour	Intravenous bolus or infusion	Contraindications: asthma, heart failure, diabetes May result in hyperkalaemia and hypoglycaemia Does not induce reflex tachycardia
Hydralazine*	Bolus: 0.2–0.6 μg/kg up to a maximum dose of 20 mg	Intravenous or intramuscular bolus	Often reflex tachycardia, fluid retention, headaches Intravenous boluses should be given every 4 hours
Esmolol	Infusion: 100–500 μg/kg/min, up to 1000 μg/kg/min	Intravenous infusion	May result in bradycardia Contraindications: asthma, heart failure Very short duration of action
Enalaprilat*	Bolus: 5–10 μg/kg up to a maximum dose of 1.2 mg	Intravenous bolus	May result in long-lasting hypotension, hyperkalaemia or acute renal failure Limited indications
Fenoldopam*	Infusion: 0.2–0.8 μg/kg/min	Intravenous infusion	Little experience in children
Sodium nitroprusside*	Infusion: 0.5–10 μg/kg/min	Intravenous infusion	Risk of cyanide poisoning if long-term use or concomitant renal or hepatic failure Need to monitor cyanide levels during long-term use (> 48 hours)
Phentolamine*	Bolus: 0.05–0.1 mg/kg up to a maximum dose of 5 mg	Intravenous bolus	May result in tachycardia Drug of choice in an adrenergic crisis
Clevidipine*	Infusion: 0.5–3.5 μg/kg/min	Intravenous infusion	Contraindications: allergy to soybean and egg proteins, dyslipidaemia Few data regarding paediatric dosage

*not available in Poland; may be obtained by a special physician prescription

Table XLIV. Oral antihypertensive drugs used in hypertensive urgencies (reprinted with permission from Standardy Medyczne)

Antihypertensive drugs	Dosage	Mode of administration	Comments
Captopril	0.3–0.5 mg/kg/dose Maximum 6 mg/kg/day	Oral	Need to monitor potassium and creatinine level
Clonidine	0.05–0.1 mg/dose, may be repeated up to a maximum dose of 0.8 mg	Oral	Adverse effects: dry mouth, sedation
Isradipine	0.05–0/1 mg/kg/dose, up to a maximum dose of 5 mg	Oral	Adverse effects: dizziness, reflex tachycardia

Table XLV. Recommended doses of oral antihypertensive drugs in children

Drug class	Drug	Initial dose	Number of daily doses	Maximum dose
Aldosterone antagonists	Eplerenone*	25–50 mg/day	1–2	100 mg/day
	Spironolactone	1 mg/kg/day	1–2	3.3 mg/kg/day up to 100 mg/day
Angiotensin-converting enzyme inhibitors	Benazepril*	0.2 mg/kg/day up to 10 mg/day	1	0.6 mg/kg/day up to 40 mg/day
	Captopril	0.3–0.5 mg/kg/dose	2–3	6 mg/kg/day up to 450 mg/day
	Enalapril*	0.08 mg/kg/day	1–2	0.6 mg/kg/day up to 40 mg/day
	Fosinopril*	0.1 mg/kg/day or 5–10 mg/day	1	0.6 mg/kg/day up to 40 mg/day
	Lisinopril*	0.07 mg/kg/day up to 5 mg/day	1	0.6 mg/kg/day up to 40 mg/day
	Quinapril*	5–10 mg/day	1	80 mg/day
	Ramipril	2.5 mg/day (6 mg/m^2/day)	1	20 mg/day
Angiotensin receptor blockers	Candesartan*	0.16 mg/kg/day up to 4 mg/day	1	0.5 mg/kg/day up to 32 mg/day
	Irbesartan*	< 13 years: 75–150 mg/day > 13 years: 150–300 mg/day	1	300 mg/day
	Losartan*	0.75 mg/kg/day up to 50 mg/day	1	1.44 mg/kg/day up to 100 mg/day
	Valsartan*	0.25–2 mg/kg/day	1	4 mg/kg/day up to 320 mg/day
	Olmesartan*	2.5 mg/day	1	40 mg/day
Renin inhibitors	Aliskiren	2 mg/kg/day	1	6 mg/kg/day up to 600 mg/day
Alpha- and beta-blockers	Labetalol**	1–3 mg/kg/day	2	10–12 mg/kg/day up to 1.2 g/day
	Carvedilol	0.1 mg/kg/dose up to 12.5 mg/dose	2	0.5 mg/kg/dose up to 50 mg/day
Beta-blockers	Atenolol	0.5–1 mg/kg/day	1–2	2 mg/kg/day up to 100 mg/day
	Bisoprolol/ hydrochlorothiazide**	0.04 mg/kg/day up to 2.5/6.25 mg/day	1	10/6.25 mg/day
	Metoprolol*	0.5–1.0 mg/kg/day up to 50 mg/day	1–2	6 mg/kg/day up to 200 mg/day
	Propranolol	1 mg/kg/day	2–3	16 mg/kg/day up to 640 mg/day
Calcium antagonists	Amlodipine*	0.06 mg/kg/day or 2.5–5 mg/day	1	0.6 mg/kg/day up to 10 mg/day
	Felodipine*	2.5 mg/day	1	10 mg/day
	Isradipine	0.05–0.15 mg/kg/day	3–4	0.8 mg/kg/day up to 20 mg/day
	Nifedipine (slow release)	0.25–0.5 mg/kg/day	1–2	3 mg/kg/day up to 120 mg/day
Central alpha-agonists	Clonidine	5–10 μg/kg/day	2–3	25 μg/kg/day up to 0.9 mg/day
	Methyldopa	5 mg/kg/day	2–3	40 mg/kg/day up to 3 g/day
Diuretics	Amiloride	0.4 mg/kg/day or 5–10 mg/day	1	0.625 mg/kg/day up to 20 mg/day
	Chlorthalidone	0.3 mg/kg/day	1	2 mg/kg/day up to 50 mg/day
	Furosemide	0.5–2.0 mg/kg/dose	1–2	6 mg/kg/day up to 450 mg/day
	Hydrochlothiazide	0.5–1 mg/kg/day	1	3 mg/kg/day up to 50 mg/day
Alpha-blockers	Doxazosin	1 mg/day	1	4 mg/day
	Prazosin	0.05–0.1 mg/kg/day	3	0.5 mg/kg/day up to 50 mg/day
	Terazosin	1 mg/day	1	20 mg/day
Vasodilators	Hydralazine**	0.25 mg/kg/dose	3–4	7.5 mg/kg/day up to 200 mg/day

*approved by the FDA for the treatment of hypertension in children
**not available in Poland; may be obtained by a special physician prescription