Guidelines of the Pediatric Section of the Polish Society of Hypertension on diagnosis and treatment of arterial hypertension in children and adolescents

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Abstract

Presented recommendations are an extended and actualized version of paediatric recommendations of Polish Society of Hypertension published in 2015. Since then, new studies have appeared on this subject, introducing a new classification of hypertension, newly described principles of management in risk groups and methods of assessing hypertensive target organ damage. The presented updated recommendations included changes introduced in the 2016 European Society of Hypertension recommendations and Recommendations of Children's Memorial Health Institute in Warsaw. Recently published guidelines of American Academy of Pediatrics have been discussed.

In the presented issue of guidelines, epidemiological information on the occurrence and incidence of hypertension in developmental age was added and classification of blood pressure values was updated. Subchapters on diagnosis and organ damage assessment, principles of diagnosis and treatment of hypertension in children with diabetes, chronic kidney disease and a subsection discussing diagnostic and therapeutic difficulties with setting blood pressure targets were revised. In addition, the principles of early diagnosis of arterial hypertension in post-hospital care in children born before 33 weeks of gestation published in 2018 as recommendations of the Polish Neonatal Society have been also taken into account.

Key words: arterial hypertension, children, adolescents, newborns, recommendations

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Introduction

Arterial hypertension (AH) is one of the main potentially modifiable cardiovascular risk factors. It is also one of the main clinical problems of adult medicine, and it is one of the most common chronic diseases in adolescents. In addition to the primary form of hypertension (essential hypertension), AH is an important complication of other chronic diseases such as: type 1 diabetes mellitus (T1DM), type 2 diabetes mellitus (T2DM), chronic kidney disease (CKD),

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coarctation of the aorta, congenital adrenal hyperplasia and others.

Because T2DM is relatively rare in Caucasian children and adolescents, children with overweight and obesity, especially those with carbohydrate intolerance and insulin resistance, should be treated as a potential risk group for AH. Arterial hypertension is also increasingly important in children and adults born prematurely, especially before 33 weeks of gestation and in children born with intrauterine hypotrophy (small for gestational age, SGA) [1–3].

These guidelines are an extended and actualized version of paediatric guidelines of the Polish Society of Hypertension published in 2015 and presented in the extended version as Recommendations of the Children's Memorial Health Institute in 2016 [4]. This version of paediatric recommendations of the Polish Society of Hypertension was developed on the basis of the previously published recommendations of the Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents of the National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents (The 4th Report), the paediatric recommendations of the European Society of Hypertension (ESH) published in 2009 and 2016, the recommendations of the Children's Memorial Health Institute (2016), the recommendations of the European Society of Cardiology (ESC)/American Heart Association (AHA) (2017), the recommendations of the American Academy of Pediatrics (AAP) (2017), literature review and expert opinions [5–8].

Compared to paediatric 2015 Guidelines of the Polish Society of Hypertension, this version contains more epidemiological information on the prevalence and incidence of AH at developmental age, expanded or modified subchapters on diagnostics and assessment of organ damage, AH in children with diabetes and CKD, and a subchapter discussing diagnostic and therapeutic difficulties. New subchapter has been added describing the principles of early diagnostics of AH in post-hospital care of children born before the 33 weeks of pregnancy, which were published in the 2018 guidelines of the Polish Neonatal Society. An important novelty is the new classification of AH presented earlier in the 2016 ESH Guidelines and recommendations of the Children's Memorial Health Institute published in 2016.

The new subchapter discusses problems with setting blood pressure targets. The chapter on the principles of blood pressure measurement gives new recommendations on how to measure blood pressure in newborns, infants and young children. References has been updated and expanded.

Epidemiology of hypertension in children and adolescents

Data from representative population studies indicate that hypertension is present in 3–5% of children and adolescents aged 0–18 years. 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 found in 6.9% of children aged 3–6 years, 7.7% of children aged 6–10 years, and 6.2% of youths aged 10–20 years [6].

The prevalence of AH in Polish adolescents aged 14–18 years (in 18-year-olds AH was diagnosed according to the definition for adults, i.e. as the blood pressure value ≥ 140/90 mmHg) reaches the values found in young adults aged 20–30 years, i.e. 10–13% [9–11]. From puberty and on, AH is 3–4 times more frequent in boys than in girls. This proportion is observed up to the 5th decade of life and is associated with physiological pressure increase during puberty in boys. In risk groups, such as patients with obesity, CKD, T1DM and T2DM, the prevalence of AH is much higher and ranges from 5–25% (T1DM) to 30–40% (T2DM). The group of particularly high risk of AH development is prematurity and low birth weight. Estimates indicate that AH was diagnosed at the age of 3 in 7.3% of prematurely born children. The risk of developing AH increases with a younger gestational age and is particularly high in those born before 33 weeks of pregnancy [12].

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.

Recommendations regarding screening for hypertension

According to the ESH guidelines (2009 and 2016) and the Fourth Report of the National High Blood Pressure Education Program Working Group on Children and Adolescents, BP should be measured in children ≥ 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 I) [5, 13]. Screening for hypertension in children below 24 months of age is not supported by society guidelines and epidemiological study findings [14]. 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.

Diagnosis of hypertension

Definitions and classification of hypertension in children and adolescents

According to the generally accepted definition of hypertension in children, this diagnosis requires BP readings ≥ 95th percentile for age, gender, and height during three separate visits. The literature also uses the term "elevated blood pressure", which refers to children who have a blood pressure value greater than 95th percentile only on one occasion, which does not allow the diagnosis of AH. The meaning of the term "elevated blood pressure" changed when the 2017 AAP guidelines adopted this term to describe the value of arterial blood pressure in the range previously referred to as prehypertension.

Classification of hypertension in children and adolescents depends on the method of BP measurement.

Due to discrepancies in the interpretation of arterial blood pressure in adolescents (see below), in youths aged ≥ 16 years it is recommended to use the same classification as in adults. 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; in children and adolescents ≥ 16 years of age BP values < 130/85 mmHg are considered as normal;
- **High normal BP (Europe)/ elevated blood pressure (USA)** — systolic blood pressure (SBP) and/or diastolic blood pressure (DBP) values between the 90th and 95th percentile, and BP within the range of 130–139/85–89 mmHg in adolescents aged ≥ 16 years (note: In the AAP classification, elevated blood pressure denotes BP values in the range 120/80–129/80 mmHg for those ≥ 13 years of age or ≥ 90th percentile and lower than 130/80 mmHg for those younger than 13 yrs);
- **Hypertension** — mean SBP and/or DBP values ≥ 95th percentile for age, gender, and height in at least 3 independent measurements; in adolescents aged ≥ 16 years threshold values are the same as in adults, i.e. ≥ 140/90 mmHg;
- **White coat hypertension** — office BP measurements above the 95th percentile or BP ≥ 140/90 mmHg in adolescents aged ≥ 16 years, but home BP or ambulatory blood pressure monitoring (ABPM) values within normal limits;

Table I. 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.**
- 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 mmHg, and at a later age they are higher by about 30–40 mmHg.
- 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 40% 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 mmHg.
- 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 mmHg, 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), increased intracranial pressure.

Table II. Blood pressure classification in children based on office blood pressure measurements

	0–16 years	≥ 16 years
BP category	**SBP and/or DBP percentile**	**SBP and/or DBP readings**
Normal BP	< 90th percentile	< 130/85 mmHg
High normal BP/pre-hypertension	≥ 90th and < 95th percentile	130–139/85–89 mmHg
Hypertension	≥ 95th percentile	≥ 140/90 mmHg
Grade 1 hypertension	95th–99th percentile + 5 mmHg	140–159/90–99 mmHg
Grade 2 hypertension	> 99th percentile + 5 mmHg	160–179/100–109 mmHg
Grade 3 hypertension		≥ 180/110 mmHg
Isolated systolic hypertension	SBP ≥ 95th percentile and DBP < 90th percentile	≥ 140/< 90 mmHg

- **Grade 1 hypertension** — BP values between the 95th percentile and 5 mmHg above the 99th percentile for age, gender, and height or BP values in the range of 140–159/90–99 mmHg in adolescents aged ≥ 16 years;
- **Grade 2 hypertension** — BP values more than 5 mmHg above the 99th percentile for age, gender, and height or BP values in the range of 160–179/100–109 mmHg in adolescents aged ≥ 16 years;
- Because in adolescents aged ≥ 16 years it is recommended to use the same classification as in adults, additional category of **grade 3 hypertension** has been specified — BP values ≥ 180/110 mmHg in adolescents aged ≥ 16 years;
- **Isolated systolic hypertension** — SBP values ≥ 95th percentile and DBP < 90 percentile; in adolescents aged ≥ 16 years: SBP values ≥ 140 mmHg and DBP < 90 mmHg (Table II).

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 purposes [15, 16]:

- **Severe hypertension** — BP values more than 30 mmHg above the 99th percentile for age, gender, and height;
- **Hypertensive urgency** — impending organ failure related to hypertension, requiring rapid intervention, usually with concomitant unspecific symptoms such as headache and vomiting;
- **Hypertensive emergency** — 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;
- **Malignant hypertension** — previously, this term was used to describe a sudden increase in blood pressure with the presence of grade 3 and/or grade 4 retinopathy on fundoscopy, which in the current classification corresponds to hypertensive emergency. According to the nomenclature proposed in the 2016 ESH guidelines, malignant hypertension is defined as a sudden increase in blood pressure accompanied by damage to at least three target organs or microangiopathy. In practice, this applies to hypertension in the course of an acute episode of the haemolytic-uremic syndrome;
- **Resistant hypertension** — blood pressure that remains above goal in spite of the concurrent use of 3 antihypertensive agents, including a diuretic.

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 III) [17]. Since, as in office blood pressure measurements, the values of blood pressure of 95th percentile obtained using ABPM in adolescents may exceed the values considered normal in adults, according to the 2016 ESH guidelines, we recommend using 95th percentile thresholds in children and adolescents, if they do not exceed the upper limit of normal values for adults. If the 95th percentile values are above the adult normal range, it is recommended to use cut-off points for adults, i.e. 130/80 mmHg for the mean 24-hour BP, 135/85 mmHg for daytime (waking) BP values and 120/70 mmHg for nighttime BP values.

Reference blood pressure values

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

Table III. Blood pressure classification in children based on ABPM [17]*

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%
Prehypertension/High normal BP	≥ 90th percentile and/or > 120/80 mmHg	< 95th percentile	25–50%
Ambulatory hypertension	≥ 95th percentile	≥ 95th percentile	25–50%
Severe ambulatory hypertension	≥ 95th percentile	≥ 95th percentile	> 50%

*For patients ≥ 16 years of age, it is recommended to use adult cut-off point, i.e. 130/80 mmHg for the mean 24-hour BP, 135/85 mmHg for the daytime (awake) and 120/70 mmHg for the nighttime (sleep) BP values.
ABPM — ambulatory blood pressure monitoring

values for children aged 0–18 years, developed for the population of the United States, Canada, Mexico, and Great Britain and published in The 4th Report [18]. For oscillometric (automated) BP measurements reference values developed for the Polish population of children aged 3–18 years are recommended [9]. Due to the fact that in paediatric practice the most commonly used measurement method is automatic measurement, these standards have been included in the "new" Child Health Record Book (2016).

Home blood pressure measurements

In children with the diagnosis of hypertension, home BP measurements (HBPM) using a validated oscillometric device are recommended (https://nadcisnienietetnicze.pl/ptnt/wytyczne_ptnt). Use of the reference values developed by Stergiou et al. for children and adolescents aged 6–18 years is recommended (Table IV) [19, 21]. 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. It is recommended to perform 2–3 measurements at short intervals and to record the value of the last measurement. The optimal assessment is based on morning and evening measurements performed in the consecutive 7 days. Adequate home BP measurements are considered a reliable indicator of the effectiveness of antihypertensive therapy [20].

Ambulatory 24-hour blood pressure monitoring

Ambulatory BP monitoring (ABPM) using a validated oscillometric device is recommended in all children above 5 years of age and higher than 119 cm in whom hypertension was diagnosed based on office BP measurements. The reference BP values for ABPM developed by Wühl et al. and adopted in the 2014 AHA guidelines should be used, and in adolescents > 16 years of age — reference values for adults. Routine repeated ABPM is recommended to evaluate treatment effects [17].

Table IV. Referential home blood pressure values (95th percentile) in boys and girls [18, 20]

Height	Girls	Boys
120–129	119/74	199/76
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

Principles of blood pressure measurement

The technique for measuring blood pressure is presented in Table I. For routine measurements, automatic (oscillometric) and auscultatory measurements can be used, and if elevated BP is detected by an automatic method, it should be confirmed by auscultatory BP measurement. Other rules apply to newborns and young children, in whom the auscultatory measurement is technically difficult and associated with a larger white-apron effect than the automatic (oscillometric) measurement. In this age group (up to 3–4 years of age) it is recommended to perform multiple automatic measurements in short intervals. In addition, in neonates and small infants who have indication for blood pressure measurement, it is recommended to perform measurements according to the protocol described in the section "Arterial hypertension in the newborn" (Table XVIII).

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 mmHg lower than 140/90 mmHg. The latter values correspond to 99th percentile in girls aged 18 years. Another phenomenon concerning adolescents is isolated systolic AH observed especially in boys without significant additional risk factors, often practicing sports. In these cases, the so-called spurious hypertension should be taken into account in which elevated systolic blood pressure is found only on the peripheral arteries, e.g. on the brachial artery, while the central pressure is normal. There are also no signs of organ damage in these cases. Therefore, when interpreting BP values, consideration should also be given to exposure to cardiovascular risk factors (intermediate phenotype) and the presence of subclinical organ damage (see below).

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 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.

On the other hand, in tall children and adolescents 95th percentile values may exceed the reference range adopted for adults. The mentioned problems were the reason for the change in the definition and classification of AH in adolescents aged ≥ 16 years old (see Diagnosis of hypertension).

Problems with setting blood pressure targets in children on antihypertensive treatment

Hypertension literature, including the ESH guidelines, the 4th Report, the AAP guidelines, expert position statements, defines the blood pressure threshold above which the AH is diagnosed and the threshold of blood pressure target values. These threshold values are different. Namely, AH is diagnosed when BP values are equal to or exceeding 95th percentile, whereas at the same time it is recommended for patients without additional cardiovascular risk factors to lower blood pressure to values below 90th percentile. The adoption of such blood pressure target values should, however, entail a change in the definition of AH and establishing a lower diagnostic threshold, i.e. a value of 90th percentile. There is a need to determine the principles for management of patients with blood pressure values of 90th–95th percentile.

This makes interpretation difficult, as it implies the introduction of treatment in children with blood pressure in the 90th–95th percentile range. While non-pharmacological treatment is not a problem, it should be considered whether to implement pharmacological treatment in patients with persistent high normal pressure despite non-pharmacological treatment. Thus, it would also be logical to change the definition of AH.

Indirect evidence that blood pressure targets for children with primary AH and without other conditions should be set at 90th percentile provide results of studies performed in adult hypertensive patients, especially SPRINT [21] and published in 2016 meta-analysis of trials assessing the effectiveness of antihypertensive treatment in risk groups such as patients with CKD and diabetes [22]. The analysis of the results of Cardiovascular Risk in Young Finns Study provides arguments for both modifying the definition of AH in children and changing the threshold of blood pressure target values to 90th percentile. The study showed significantly higher blood pressure and higher arterial stiffness, assessed as the pulse wave velocity, in adult patients who had high normal blood pressure values (i.e. between 90th and 95th percentile) in childhood and adolescence compared with those who in childhood and adolescence had blood pressure below 90th percentile [23].

In the AAP [24] recommendations published in 2017, based on the results of the SPRINT study, new AH definitions were proposed. Lower blood pressure targets (below 90th percentile or below 130/80 mmHg) were also recommended in children with primary AH, arguing that lowering blood pressure below these values leads to a further reduction in left

ventricular hypertrophy. It should be noted, however, that the SPRINT study examined the population of patients with mean age of 67 years who were previously treated with antihypertensive drugs and were already burdened with additional diseases. Moreover, the blood pressure measurement method was different from that used in clinical practice. Also, the papers cited in the AAP guidelines do not report further reduction of left ventricular mass in children whose blood pressure was lowered below 90th percentile [25]. It should also be noted that in children and adolescents with primary AH the strongest predictor of the reduction of left ventricular mass and the incidence of left ventricular hypertrophy is not a decrease in blood pressure values, but visceral fat reduction, expressed as waist circumference reduction, and normalization of metabolic disorders [26]. Taking the above into consideration, in the presented guidelines for children and adolescents with primary AH and without additional diseases, we recommend blood pressure levels lower than 95 percentile (or below 140/90 mmHg). At the same time, we recommend intensive non-pharmacological treatment as a basic therapeutic option in primary AH and in children with high-normal BP.

Similar difficulties are related to the diagnosis threshold for AH and recommended target BP values in children with CKD and children with diabetes. In children with CKD, pharmacological treatment is recommended when blood pressure exceeds 90th percentile, and the target BP values depend on the presence of proteinuria. The current recommendations are based on the results of the ESCAPE study, which showed that in children with proteinuria > 0.5 g/day, a reduction in mean arterial blood pressure in the ABPM measurement below 50th percentile is beneficial. However, these benefits have not been demonstrated for children with lower proteinuria or no proteinuria. The ESH guidelines and expert position statements (review articles) recommend that in these cases the target pressure values should be below 75th percentile, although even the papers cited in these documents do not provide any justification for such a recommendation. Nevertheless, because there is strong pathophysiological link between proteinuria, even small, and progression of CKD, we recommend to try to lower BP below 50th percentile for 24h MAP if it is tolerated, in all patients with CKD. Similar recommendations have been endorsed by AAP.

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.

Evaluation of left ventricular mass

Left ventricular mass (LVM) is a major criterion of target organ damage. 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 (nevertheless, it is a study that allows to detect arrhythmias and myocardial ischemia, which is of practical importance, because non-pharmacological treatment based on physical exercise/ /sport is the basic therapy for primary AH). 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 de Simone. Published reference values and percentiles of the LVM index calculated using this formula allow using this parameter in children over 1 year of age [27]. 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 recommended (ESH 2009, 2016, the 4th Report, AAP) 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. However, due to the introduction of AH classification for adolescents aged ≥ 16 years that is consistent with the definitions used in adults, in this age group of adolescents it is recommended to diagnose left ventricular hypertrophy according to the criteria for adults (see below).

The assessment of left ventricular systolic and diastolic dysfunction is not different from that used in adults. When assessing diastolic function, it should be taking into account early (E) filling wave to atrial (A) wave (E/A) ratio is higher in younger children [28–30]. The assessment of left ventricular diastolic function based on tissue Doppler examination is increasingly being used and relevant paediatric reference values have been published [31]. The results of this study may be an additional parameter for the assessment of target organ damage.

Definitions:
— left ventricular hypertrophy — LVM index ≥ 95th percentile for age and gender;
— severe left ventricular hypertrophy — LVM/ /height$^{2.7}$ index ≥ 51 g/m$^{2.7}$*.

In adolescents aged ≥ 16 years left ventricular hypertrophy is diagnosed when LVM/body surface area (BSA) is > 115 g/m^2 for boys and > 95 g/m^2 for girls.

It is recommended to assess the relative thickness of the left ventricle wall (threshold value 0.42) and determine the geometry of the left ventricle (normal geometry, concentric remodelling, concentric hypertrophy, eccentric hypertrophy).

*Observations of adult populations showed that LVM/ /height$^{2.7}$ index over 51 g/m$^{2.7}$ was associated with a 4-fold higher risk of a cardiovascular event over a 5-year period. The value of 51 g/m$^{2.7}$ corresponds to approximately 99th percentile of LVM in children and adolescents [32].

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 [30, 32]. Computer analysis of retinal arterial and venous diameter is increasingly used in the assessment of risk of cardiovascular events, including stroke in adults with AH, but still is not commonly used in children with AH [33, 34].

Although the initial assessment of the fundus is relatively simple, in clinical practice, few paediatric hypertension specialists perform fundoscopic examination. Therefore, fundoscopy is suggested as an optional examination in the diagnosis of children and adolescents with asymptomatic AH, but is recommended as a routine diagnostic method in symptomatic AH and hypertension urgency and emergency.

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 in subjects with normal GFR is considered as an abnormality specific for primary hypertension. However, it is not clear whether increased serum uric acid concentration is a primary phenomenon or occurs secondarily to subclinical renal damage [35, 36]. Clinical trials and population studies show that in adolescents aged 12–17 years, uric acid > 5.5 mg/dl is associated with a 2-fold higher risk of primary hypertension.

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:
— assessment of carotid intima-media thickness (cIMT);
— measurement of the pulse wave velocity (PWV).

During the last decade, multiple reports have been published that support using cIMT and PWV measurements to evaluate target organ damage, and pediatric reference values for cIMT and PWV have been published (Table V and VI) [37–42]. These tests are already recommended (ESH 2016) as additional in the assessment of target organ damage in children with AH. However, the assessment of cIMT and PWV is still performed only in a few centres. Therefore, until these methods are commonly used in clinical practice, we recommend them as non-obligatory.

Principles of the differential diagnosis of hypertension in children and adolescents

Differential diagnosis of hypertension in children includes three steps (Table VII). 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, i.e. below average age of pubertal growth spurt), and/or grade 2 hypertension and/or presence of target organ damage and/ /or concomitant chronic conditions. Diagnostic step 1 includes confirmation of the diagnosis of hypertension, exclusion of white coat hypertension, classification and grading the severity of hypertension, evaluation of target organ damage, and basic laboratory tests to exclude secondary hypertension. Diagnostic step 2 includes tests that usually require hospital admission, but if possible may be done also on outpatient basis, and is generally appropriate in children with grade 2 hypertension and younger

Table V. Reference values of common carotid artery intima-media thickness (cIMT) in millimetres — 50th and 95th percentile [42]

	50th percentile [mm]		95th percentile [mm]	
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	0.40	0.39	0.48	0.46
17	0.40	0.39	0.48	0.46
18	0.40	0.39	0.48	0.47

Table VI. 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®) [39]

Age (years)	PulsePen® (tonometry) Boys 95th percentile [m/s]	PulsePen® (tonometry) Girls 95th percentile [m/s]	Vicorder® (oscillometry) Boys 97th percentile [m/s]	Vicorder® (oscillometry) Girls 97th percentile [m/s]
7	5.4	5.23	4.82	4.82
8	5.45	5.4	4.96	4.98
9	5.51	5.54	5.1	5.14
10	5.61	5.68	5.24	5.27
11	5.75	5.81	5.38	5.39
12	5.91	5.91	5.52	5.5
13	6.09	6.0	5.67	5.59
14	6.27	6.0	5.82	5.66
15	6.47	6.19	5.98	5.67
16	6.67	6.31	6.16	5.65
17	6.87	6.46	6.34	5.63
18	7.08	6.65		
19	7.28	6.85		

children with AH. 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 AH 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, and ABPM is performed in exceptional, individually qualified cases.

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. Except for hypertensive urgencies and

Table VII. Diagnostic steps in children with hypertension

	Investigations	Comments
Step 1	• complete blood count, creatinine, sodium, potassium, chloride, calcium, bicarbonate, total cholesterol, triglycerides, cholesterol fractions, uric acid, glucose • urine analysis and urine culture • daily albumin excretion or albumin/creatinine ratio in a spot urine sample • kidney and renal artery Doppler ultrasound • ECG • echocardiography with evaluation of left-ventricular mass and the aortic arch • measurement of carotid intima-media thickness (cIMT) • transfontanellar ultrasound in neonates • ABPM in children > 5 years	Step 1 investigations should be performed in all patients with the diagnosis of hypertension cIMT measurement is optional 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 • 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 • thyroid hormones, vitamin D3 metabolites • renal scintigraphy (captopril test) in younger children and all patients with grade 2 hypertension	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 state 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 steroid profile is currently recommended over previously used urinary 17-keto- and 17-hydroxysteroids Measurements of thyroid hormones and vitamin D_3 metabolites in patients with a suspicion of specific pathologies Dynamic scintigraphy is recommended to evaluate renal perfusion, urine excretion, split 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 (computed tomography angiography, magnetic resonance angiography, invasive angiography) • diagnostic imaging of adrenal pathology/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; DMSA — dimercaptosuccinic acid; ECG — electrocardiogram; HOMA-IR — homeostatic model assessment-insulin resistance; cIMT — carotid intima-media thickness

emergencies, if pharmacological 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 [43].

General approach to the treatment of hypertension in children and adolescents

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 1). Antihypertensive pharmacological treatment and its success rates depend on the aetiology of hypertension.

Hypertension in chronic kidney disease

In the paediatric population, hypertension secondary to CKD 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. The prevalence of AH increases with decreasing values of glomerular filtration rates (GFR). Hypertension is more common in children with CKD caused by glomerulopathy and practically all who have developed CKD due to haemolytic-uremic syndrome. Hypertension affects up to 80% children on dialysis (stage 5 CKD). The pathogenesis of AH in the course of CKD involves both the renin-dependent and hypervolaemic mechanisms. As GFR decreases, the contribution of sodium and water retention to the pathogenesis

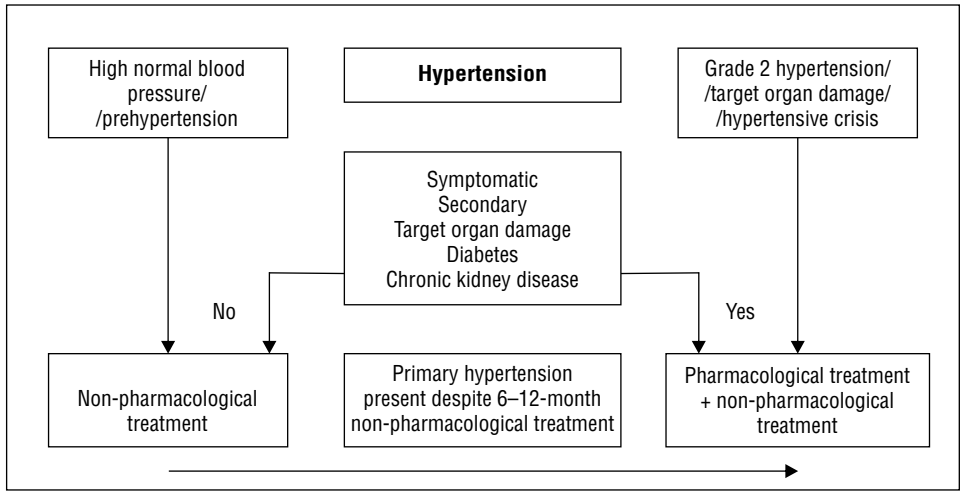

Figure 1. Principles of therapeutic approach to hypertensive child

of AH in patients with CKD becomes more and more important. Inadequately controlled AH is an important cause of deaths occurring during renal replacement therapy due to cardiovascular complications. Moreover, AH is the primary factor of CKD progression, along with proteinuria. 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. However, in both 2009 and 2016 ESH guidelines the BP threshold at which treatment should be started has been defined ambiguously. Based on randomized prospective studies, clinical observations, expert opinions, and the results of recently published meta-analyses of studies in adults, it should be assumed that antihypertensive treatment should be initiated in children with CKD whose blood pressure values exceed 90th percentile. It is recommended to monitor antihypertensive treatment by ABPM, and treatment effectiveness should be evaluated bases on the mean 24-hour MAP. Target BP values depend on the severity of proteinuria. Reduction of the mean 24-hour MAP below the 90th percentile (range 50th–90th percentile) is recommended in children with chronic kidney disease without proteinuria or with proteinuria below 0.5 g per day, and in children with proteinuria over 0.5 g per day 24-hour MAP should be lower than the 50th percentile [44, 45]. However, because there is linear relationship between proteinuria and progression of CKD, it is also recommended to try to lower 24h MAP values below 50th percentile in all children with CKD if such treatment is well tolerated [24].

First-line antihypertensive drug classes in children with chronic kidney disease are RAAS inhibitors: angiotensin converting enzyme blockers (ACEI) and angiotensin II type 1 receptor blockers (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 [46].

Achieving target BP in patients with chronic kidney disease usually requires multiple antihypertensive drugs. Individualization of further pharmacological 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, reduction of proteinuria and adrenergic drive. 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 in proteinuric patients, due to the fact that they increase proteinuria and hyperfiltration. This negative effect is absent or reduced in combination with RAAS inhibitors [47].

Hypertension in patients on dialysis therapy

Hypertension in children with CKD requiring renal replacement therapy is found in 55–79% of patients, including 56–79% treated with haemodialysis, 54–75% treated with peritoneal dialysis (in Poland, 56% and 54%, respectively), as well as around 66% of patients after kidney transplantation [48–50]. It should be noted that approximately 20% of dialyzed children with hypertension are untreated, and among those undergoing treatment, nearly 75% of children have poorly controlled hypertension [48]. Since the assessment of blood pressure measurements performed in Dialysis Wards (before and after haemodialysis) to a lesser extent correlates with left ventricular hypertrophy than 24-hour ABPM in the inter-dialysis period, the diagnosis of AH in children on chronic haemodialysis should be based on 24-hour ABPM in the period between dialysis sessions. The main risk factor for AH in chronically dialysed children is overhydration and excessive salt supply. Other risk factors are: young age of the child (< 6 years), black race, female gender, acquired underlying kidney disease, anaemia and the duration of dialysis therapy (the longer the time, the smaller the percentage of patients with high blood pressure) [48–52]. The most important element of AH prevention and treatment in children undergoing dialysis is a correct assessment of the hydration status and achieving dry body weight [53–57]. It is believed that the weight gain between dialysis sessions in children should not exceed 3% of dry body weight. In children on peritoneal dialysis the main cause of hypervolaemia is the so-called latent hypervolaemia associated with uremic cachexia and malnutrition-inflammation-arteriosclerosis syndrome [58]. The volume of residual diuresis plays a significant role in these patients — the higher the residual diuresis, the lower BP values in hypovolaemic hypertensive patients [59].

According to the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKD KDOQI) guidelines published in 2005, target BP values in children requiring chronic renal replacement are < 95th percentile for sex, age and height [60]. Appropriate dry body weight can be achieved by intensifying dialysis: extending the time of dialysis session to 5–8 hours, performing 4–6 sessions per week, using periodic haemodiafiltration and/or nocturnal dialysis [61, 62]. In patients on peritoneal dialysis, higher ultrafiltration can be achieved by using dialysis fluids with higher osmolality or fluids containing icodextrin [63]. Pharmacological treatment involves the use of dihydropyridine calcium antagonists, ACEI and ARB [64]. There are no explicit recommendations regarding the choice of the drug. It should be remembered, however, that the treatment with ACEI and ARB is associated with the risk of hyperkalaemia.

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%) [65–67]. 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 [68–69].

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 2). Invasive angiography, often with selective renal artery catheterization, continues to be a reference method but should be performed only if percutaneous treatment, during the same procedure, is planned based on the results of non-invasive imaging. It should be noted that in children and adolescents with renovascular hypertension, the sensitivity and specificity of non-invasive imaging tests, such as Doppler ultrasound (73%, 83%), nuclear magnetic resonance

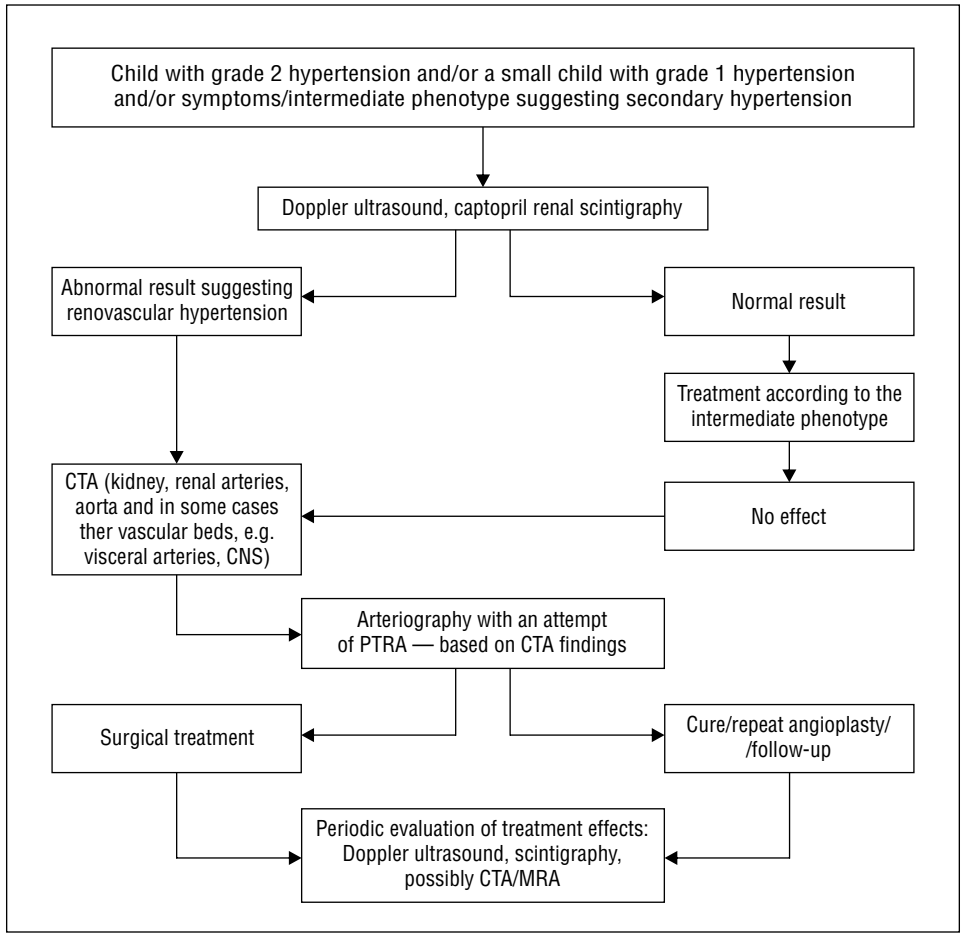

Figure 2. Diagnosis and treatment in children with renovascular hypertension

angiography (80%, 62%) and computed tomography (93%; 81%), are significantly lower than that of the classic arteriography, which is regarded as gold standard method [70].

Routine evaluation of renal vein renin activity or level is not recommended. This test may be performed in case of diagnostic uncertainties.

Scintigraphy is not recommended in AAP guidelines or in clinical guidelines for adult patients, including the guidelines of the Polish Society of Hypertensions, in the diagnostic algorithm for renovascular hypertension in adults [4, 24]. However, in our opinion the assessment of split renal function and analysis of perfusion curves helps in deciding on surgical treatment in difficult cases (young children in whom percutaneous treatment is impossible), allows the evaluation of the treatment effects after interventional procedures (percutaneous treatment/surgery) and is an additional criterion for the diagnosis of hypertensive nephropathy in a kidney with normal renal artery and exposed to high blood pressure before treatment [71].

Treatment of renovascular hypertension

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

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

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

Table VIII. Pharmacological treatment of renovascular hypertension

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

or without stenting. PTRA is the initial step of the interventional treatment and it should be attempted during 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, nitroglycerine, 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 [72].

Experience with stenting in renovascular hypertension in children and adolescents is relatively limited [73]. 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.

Surgery is considered as a last resort in the treatment of renovascular hypertension. Two major approaches to the surgical treatment of renovascular hypertension are revascularization and nephrectomy. Surgical revascularization is indicated if pharmacological therapy and PTRA were unsuccessful, and nephrectomy is indicated for unilateral RAS with severely impaired function of the ischemic kidney, with reduction of size of 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.

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 [74–77].

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 pharmacological therapy and possible diagnostic investigations for recoarctation. In patients after invasive treatment (surgical or endovascular) of CoA in whom AH is still present or developed after period of normotension, ABPM should be regularly done to assess treatment efficacy. According to the recommendations of both AHA and ESC, the assessment of postoperative anatomy of the aorta, including aortic arch configuration, as factors affecting the recurrence and severity of AH, requires periodic imaging examinations (depending on age ECHO, CT, MRI patient), performed usually every few years [78, 79]. In patients with coarctation of the aorta and coexistence of a bicuspid aortic valve, the monitoring must additionally include the evaluation of anatomy and potential aortic valve dysfunction and the degree of ascending aorta dilatation. In these patients, AH treatment should be particularly aggressive.

Monogenic hypertension

The diagnosis of monogenic hypertension is based on the detection 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 (Table IX). The diagnosis of a specific form of the disease usually allows introducing a treatment targeted to the main disorders leading to the development of AH [80–88]. Diagnosis and treatment of these forms of AH should be carried out in reference centres where molecular diagnostics can be performed.

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 X) [89, 90]. Besides the presence of metabolic disorders directly related to visceral obesity, primary hypertension is characterised by the tendency to higher uric acid levels. 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.

Non-pharmacological therapy including both dietary modifications and physical activity is of major importance in the management of primary hypertension. Daily high- to moderate-intensity exercise for 60 to 90 minutes is recommended. There are no contraindications to practicing certain types of sport/physical activity. Dietary management is not different from that used in the prevention and treatment of obesity. In addition to the restrictions on the size, composition and caloric content of meals, it is important to drastically limit the intake of table salt, which means essentially eliminating adding salt to foods.

Pharmacological therapy should be considered in children with grade 1 hypertension in whom BP was not adequately lowered despite 6–12 months of non-pharmacological therapy and is indicated in children with grade 2 hypertension and/or target organ damage. Due to concomitant metabolic disturbances and mechanism of action (increase in peripheral vascular resistance), 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, instead of RAAS inhibitors, new generation beta-blockers with vasodilatory properties may be used, as these drugs do not induce adverse metabolic effects and do not increase peripheral vascular resistance, and dihydropyridine calcium antagonists. 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 [91].

Hypertension in children with diabetes

Currently, about 205,000 people suffer from type 1 diabetes (T1DM) in Poland, of which more than 20,000 are children and adolescents. In addition, a four-fold increase in the incidence of T1DM has been observed over the past 25 years [92]. With the increase in the prevalence of overweight and obesity, the number of children with type 2 diabetes (T2DM) is also increasing in the Polish population [93].

Based on the few studies in which the diagnosis was based on a generally accepted paediatric definition, the prevalence of AH in children with T1DM is estimated at 4–7%, whereas this complication is present in as much as 23–40% of paediatric patients with T2DM [94–96]. In this group of patients there is also a higher prevalence of metabolic disorders and metabolic syndrome, which is related to the pathogenesis of T2DM. Although AH most often affects patients with T2DM, its prevalence in children and adolescents with T1DM becomes increasingly common clinical problem [97, 98]. AH is one of the main risk factors for the development of micro- and macrovascular complications, cardiovascular disease, and diabetic kidney disease which are the main causes of morbidity and mortality in patients with T1DM and T2DM [99, 100].

Pathogenesis of hypertension in children with diabetes

The pathogenesis of AH in children with T1DM is not fully understood. Comparison of the clinical picture of children with primary hypertension and children with T1DM and AH indicates the involvement of common pathogenetic mechanisms, such as overweight and obesity, disorders of body fat distribution, and associated insulin resistance. Poor diabetes control and use of higher doses of insulin are also significant factors [101]. As in the general population, in children with T1DM significant increase in AH incidence is observed from puberty and on.

Table IX. Monogenic forms of hypertension — intermediate phenotype, inheritance pattern, treatment

Form of monogenic hypertension	Gene	Inheritance	Inermediate phenotype	Serum potassium	Serum bicarbonates	Plasma renin activityrenin concentrations	Serum aldosterone	Other clinical and biochemical abnormalities	Treatment
Liddle syndrome	*SCNN1A, SCNN1B, SCNN1G*	AD	Variable clinical expression	↓–	↑	↓	↓		Amiloride, triamteren
Apparent mineralocorticoid excess	*HSD11B2*	AR	Often low birth weigth, prematurity, hypercaliuria, nephrocalcinosis, AH may be present already in infancy. 4 variants of disease	↓–	↑	↓	↓	Excessive urinary excretion of metabolites of cortisol in relations to metabolites of cortisone	Amiloryd, triamteren, spironolakton/eplerenon, small doses of dexamethasone, thiazides in case of hypercalciuria
Psuedohypoaldosteronizm type II	*WNK1, WNK4 KLHL3 CUL3*	AD, AR	Clinical expression depends on type of mutation	↑	↓	↓–	↓–	Hypercalciuria, normal GFR	Thiazides
Mineralocorticoid receptor mutation S810L	*NR3C2*	AD	In women AH may appear or exaggerate in the second trimester of pregnancy; spironolactone may casue rise of blood pressure	↓–	↑	↓	↓		Amiloride, triamteren, thiazides
Familial hyperaldosteronim type I	*CYP11B2*	AD	Develops already in childhood	↓	↑	↓	↑	Hybrid steroids in urine	Dexsamethasone, eplerenon/spironolacton
Familial hyperaldosteronim type II	*CLCN2*	AD	AH may be diagnosed in infance but usually develops in second or third decade of life	↓	↑	↓	↑	Uni- or bilateral adrenal hyperplasia	Spironolactone/eplerenon, adrenalectomy
Familial hyperaldosteronim type III	*KCNJ5*	AD	Variable clinical expression, severe hypertension may be present already in early childhood; Type A — severe clinical course, bilateral adrenalectomy may be required; Type B — more benign, pharmacological treatment may be effective	↓	↑	↓	↑	Hybrid steroids may be present in urine; bilateral adrenal hyperplasia may develop Type A — severe clinical course, bilateral adrenalectomy may be requiered Type B — more benign, pharmacological treatment may be effective	Spironolactone/eplerenon, adrenalectomy
Familial hyperaldosteronim type IV	*CACNA1H*	AD	Variable clinical expression, severe AH may be diagnosed already in preschool age	↓	↑	↓	↑	No adrenal abnormalities	Spironolactone/eplerenone, angiotensin receptor blockers as additional drugs
Familial hyperaldosteronism type V (PASNA — primary aldosteronism with seizures and neurological abnormalities)	*CACNA1D*		Severe neurological abnormalities	↓	↑	↓	↑	No adrenal abnormalities	Calcium channel blockers MR antagonists
Deficiency of 11β-steroid hydroxylase	*CYP11B*	AR	AH in childhood or even in infancy; premature maturity	↓–	↑–	↓–	↓	Excessive excretion of deoxicortocisterone and testosterone metabolites; adrenal hypertrophy	Spironolactone/eplerenone, hydrcortisone
Deficiency of 17α-steroid hydroxylase	*CYP17A1*	AR	AH in childhood; delayed sexual maturation	↓–	↑–	↓–	↓	Defiiciency of sex hormones	Spironolactone/eplerenone,
Familial resistance to glucocorticoids	*GR*	AR/AD	Hypercoticosolemia without signs of Cushing syndrome	↓–	↑–	↓–	↓	Hypercoticosolemia without signs of Cushing syndrome	Spironolactone/eplerenone; dexamethasone
Brachydaktyly with arterial hypertension	*PDE3A*	AD	Short stature, brachydaktyly type E	–	–	–↑	–↑	Neurovascular conflict ; arterial anomiales in other vascular sites (renal artery stenoses	Vasodilating antihypertensive drugs

Table X. Definitions of metabolic syndrome in children according to the International Diabetes Federation 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 mmHg and/or DBP ≥ 85 mmHg — fasting blood glucose ≥ 100 mg/dL or T2DM
≥ 16 years	Criteria as in adults: Waist circumference ≥ 94 cm in boys and ≥ 80 cm in girls+ 2 or more from the following criteria: — serum HDL cholesterol < 40 mg/dL in boys and < 50 mg/dL in girls — SBP ≥ 130 mmHg and/or DBP ≥ 85 mmHg or antihypertensive pharmacological treatment — fasting blood glucose ≥ 100 mg/dL or type 2 diabetes

In patients with T1DM, abnormal circadian BP pattern, including non-dipping (lack of nocturnal BP drop) and significant morning BP surge is observed on early stage of disease. The association of elevated BP and abnormal circadian BP pattern with early markers of kidney damage suggests the involvement of both renal mechanisms and central regulation of arterial pressure [102–105]. The metabolic disorders resulting from chronic hyperglycaemia leading to atherosclerosis and increased arterial stiffness are also involved in the development of hypertension in diabetic patients [106–109].

Although, renal failure in diabetic kidney disease usually occurs after many years of disease, the early stages of diabetic kidney disease characterized by increased albuminuria are observed also in the paediatric population [110–113]. In adolescents kidney damage in T1DM is directly related to elevated BP values, and effective antihypertensive treatment slows the progression of kidney damage [114].

In children and adolescents with T2DM, AH is detected at diagnosis of diabetes in 12–25% of patients and is associated with disorders resulting from insulin resistance and abdominal obesity [115, 116]. Moreover, patients with T2DM are more frequently affected by atherogenic dyslipidaemia leading to early presence of increased vascular stiffness [117], and in those with significant obesity, kidney damage occurs before clinically overt T2DM. In some patients increased urinary albumin excretion is found at diagnosis. Due to the fact that in T2DM patients hypertension coexists with other features of the metabolic syndrome, these patients more frequently and earlier develop cardiovascular disease and nephropathy than those with T1DM. For this reason, patients with T2DM need comprehensive treatment for all disorders associated with the metabolic syndrome [118].

Diagnostic investigations for hypertension in children with diabetes

Blood pressure measurements in children and adolescents with diabetes should be performed on each visit. In children below 7 years of age BP should be measured at least twice a year [119]. In adolescents over 12 years of age with T1DM, values above 95th percentile, or above 130/80 mmHg are considered to be abnormal blood pressure regardless of the 95th percentile. 24-hour ABPM should be used to confirm the diagnosis of AH.

Due to the fact that children with diabetes are at increased risk of developing cardiovascular disease, a blood pressure reduction of ≤ 90th percentile for age, sex and height or to ≤ 120/80 mmHg is recommended regardless of age.

Lowering blood pressure leads to regression of organ damage, but too intensive treatment and lowering of diastolic pressure < 60 mmHg may impair coronary artery flow [120]. Diagnostic investigations for secondary AH in diabetic child should be performed according to the principles outlined earlier.

Diagnostic investigations for secondary AH should be performed according to the principles outlined earlier.

Treatment of hypertension in in patients with diabetes

The treatment of AH in paediatric patients should include lifestyle modification, adequate metabolic control of diabetes and pharmacological therapy. The non-pharmacological treatment including body mass normalization (BMI < 90th percentile for sex and age), regular physical activity (moderate to intense > 1 hour per day) and low sodium diet is of key importance (Table XI).

Table XI. Treatment of hypertension in children with diabetes

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

*Body weight reduction to normal values (body mass index < 90th percentile) and physical activity > 1 hour per day with home and ABPM measurements.
It is recommended to monitor the effects of treatment by home measurements and ABPM measurements, with the assessment of the night blood pressure drop

For pharmacological therapy, the recommended antihypertensive drug classes are ACEI [121] or, in case of ACEI intolerance, ARB. Pharmacological treatment should be monitored by HBPM and ABPM, and the nocturnal BP fall should be taken into consideration.

Drug classes recommended for the treatment in children and adolescents with hypertension and diabetes are ACEI [122] and, in case of ACEI intolerance, ARB. Antihypertensive treatment in children with diabetes is synonymous with renoprotective treatment and is based on similar principles. Effective pharmacotherapy in patients with diabetic nephropathy delays the development of end-stage renal failure [122]. Treatment with ACEI in adolescents is associated with long-term therapy, which can cause many adverse effects, such as cough, hyperkalaemia, headaches, impotence and the risk of pseudoallergic reactions. It should be remembered that ACEI may cause serious foetal complications, which is a significant potential problem when treating teenage girls [123].

In one-third of patients with T2DM, monotherapy with ACEI or ARB is ineffective [116]. These patients require combination therapy (second line drugs are dihydropyridine calcium antagonists, followed by vasodilating beta-blockers and thiazide diuretics)

Hypertensive urgencies and emergencies

In the developmental period, hypertensive emergencies are virtually always caused by secondary hypertension, including those casued 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, and recommendations presented in the guidelines (2009 and 2016 ESH guidelines, the 4th Report, and 2017 AAP guidelines) 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. BP should be measured every 15 minutes until it is reduced by 30% of the overall target BP reduction. 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 and aortic arch. 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 30% within the next 24–36 hours. Normal BP values (< 90th to 95th percentile) should be reached within 72–96 hours. The choice of intravenous drug depends on the aetiology of hypertension. 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 nitroglycerine) 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 be lowered by 30% of the overall

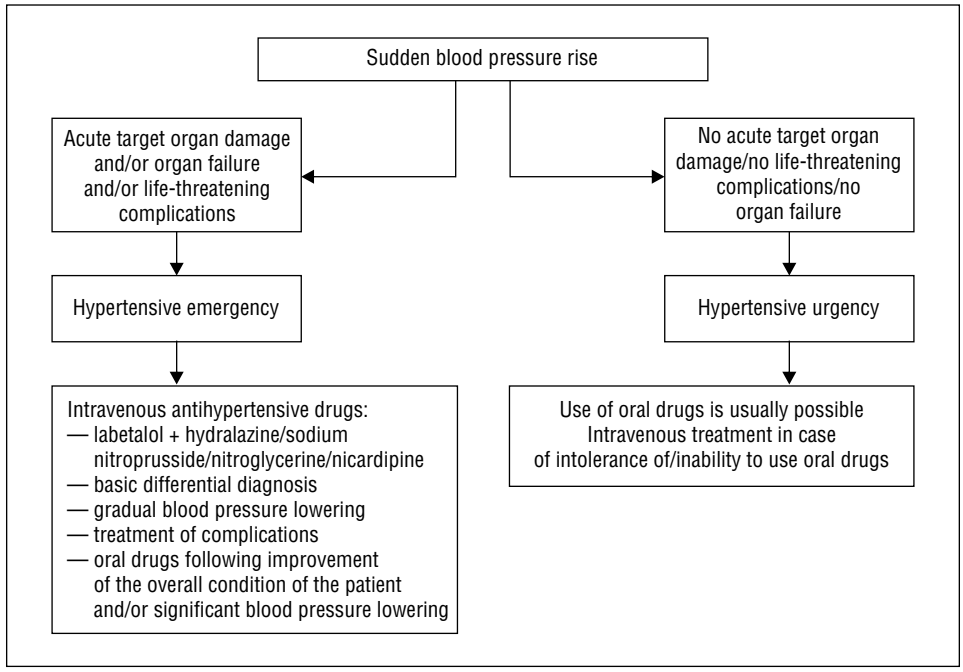

Figure 3. Management of hypertensive urgencies and emergencies in children and adolescents

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 3, and dosage of the drugs used in hypertensive emergencies, along with their adverse effects and contraindications, is summarized in Table XII and XIII. 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 [124] (Table XIV).

Other selected forms of hypertension are presented in Table XV.

Neonatal hypertension

The incidence of AH in neonates is approximately 0.2–0.3% [125, 126], but it is much higher (0.81–9%) in premature infants and in the presence of additional risk factors (umbilical vessel catheterization, patent ductus arteriosus, intraventricular haemorrhage) and associated diseases (40% in neonates with chronic bronchopulmonary disease). Neonatal hypertension is a secondary nature and is related mainly to renal pathology, most commonly renovascular diseases, but iatrogenic factors are also of major importance [127].

Despite multiple data on reference BP values in neonates depending on specific measurement techniques, the definition of hypertension is still based on the percentile values reported in the Report of the Second Task Force on Blood Pressure Control (1986) in Children and derived from BP measurements using a mercury sphygmomanometer (Table XVI). According to the 1986 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. In preterm infants, SBP values should be referred to gestational age [125, 127]. Despite many methodological reservations and the fact that currently almost exclusively oscillometric measurements are used, the reference values given in the 2nd Report are practical and easy to apply. Table XVII shows a compilation of previous reference BP values that summarizes the 95th and 99th SBP, DBP, and MAP percentiles in 2-week-old neonates, depending on gestational age [129].

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 concern preterm neonates born with concomitant congenital malformations and diseases associated with hypertension and newborns requiring hospitalization. It is recommended to perform BP measurements in appropriate

Table XII. Antihypertensive drugs used in hypertensive emergencies

Antihypertensive drugs	Dosage	Comments
Labetalol	**Bolus:** 0.2–1 mg/kg up to a maximum dose of 40 mg **Infusion:** 0.25–3 mg/kg/hour	**Contraindications:** asthma, heart failure, diabetes May result in hyperkalaemia and hypoglycaemia Does not induce reflex tachycardia **Onset of action:** 5–10 min
Phentolamine	**Bolus:** 0.05–0.1 mg/kg up to a maximum dose of 5 mg	May result in tachycardia Drug of choice in an adrenergic crisis **Onset of action:** 1–2 min
Furosemide	**Bolus:** 0.5–5 mg/kg	Need to monitor potassium levels (may cause hypokalaemia), useful in hypervolaemic hypertension **Onset of action:** 5–10 min
Hydralazine	**Bolus:** 0.2–0.6 mg/kg up to a maximum dose of 20 mg i.v. or i.m.	Often reflex tachycardia, fluid retention, headaches Intravenous boluses should be given every 4 hours. Simultaneous use of furosemide is necessary **Onset of action:** 10–20 min
Sodium nitroprusside	**Infusion:** 0.5–8 μg/kg/min	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) **Onset of action**: 1–2 min
Nitroglycerine	**Infusion:** 0.1–2 μg/kg/min	May cause methemoglobinaemia, exerts vasodilating effect mainly on veins — effective in heart failure, limited effectiveness in children **Onset of action:** 2–5 min
Esmolol	**Infusion:** 100–500 μg/kg/min, up to 1000 μg/kg/min	May result in bradycardia **Contraindications:** asthma, heart failure Very short duration of action **Onset of action:** 1–2 min
Nicardipine	**Bolus:** 30 μg/kg up to a maximum dose of 2 mg **Infusion:** 0.5–4 μg/kg/min	May induce reflex tachycardia **Onset of action:** 5–10 min
Enalaprilat	**Bolus:** 5–10 μg/kg up to a maximum dose of 1.2 mg	May result in long-lasting hypotension, hyperkalaemia or acute renal failure Limited indications **Onset of action:** 15–30 min

Table XIII. Oral antihypertensive drugs used in hypertensive urgencies

Captopril	0.1–0.2 mg/kg/dose, maximum 6 mg/kg/day	Need to monitor potassium and creatinine level **Onset of action**: 10–20 min
Clonidine	2–5 μg/kg/dose, maximum 10 μ/kg/dose	**Adverse effects:** dry mouth, sedation **Onset of action**: 30–60 min
Amlodipine	0.06–0.3 mg/kg/dose, maximum 5–10 mg/dose	**Adverse effects:** dizziness, reflex tachycardia **Onset of action**: 1–2 hours
Doxazosin*	1 mg/dose, maximum 4 mg/day	**Adverse effects:** dizziness, orthostatic hypotension **Onset of action**: 1–2 hours
Prazosin*	0.05–0.1 mg/kg/day in 3 doses, maximum 0.5 mg/kg/day	**Adverse effects:** dizziness, nausea, orthostatic hypotension **Onset of action**: 1–2 hours
Propranolol*	1 mg/kg/day in 2–3 doses maximum 4 mg/kg/day, but not exceeding 640 mg/day	**Contraindications**: asthma, bradycardia, arrhythmia, diabetes **Adverse effects:** bradycardia, bronchospasm, hypotension, Raynaud syndrome symptoms **Onset of action**: 1–2 h

*Drugs recommended in adrenergic hypertension (pheochromocytoma/paraganglioma/neuroblastoma). In these cases, BP should be lowered using alpha-blockers (doxazosin, prazosin), and then a beta-blocker (propranolol) should be initiated

Table XIV. 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	0.08–0.6 mg/kg/day	1–2	40 mg/day
	Fosinopril	0.1–0.6 mg/kg/day or 5–10 mg/day	1	40 mg/day
	Lisinopril	0.08–0.6 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	2.5–6 mg/day (6 mg/m^2/day)	1	20 mg/day
Angiotensin receptor II blockers 1	Candesartan	0.16–0.5 mg/kg/day (4 mg/day)	1	32 mg/day
	Irbesartan	75–150 mg/day	1	300 mg/day
	Losartan	0.75 mg/kg/day (up to 50 mg/day)	1	1.4 mg/kg/day up to 100 mg/day
	Valsartan	0.4 mg/kg/day	1	40–80 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	1–2	2 mg/kg/day
	Propranolol	1 mg/kg/day	2–3	4 mg/kg/day up to 640 mg/day
Calcium antagonists	Amlodipine	0.06–0.3 mg/kg/day	1	5–10 mg/day
	Felodipine	2.5 mg/day	1	10 mg/day
	Isradipine	0.05–0.15 mg/kg/dose	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	2–5 μg/kg/dose	2	10 μ/kg/dose
	Methyldopa	5 mg/kg/day	2–3	40 mg/kg/day up to 3 g/day
Diuretics	Amiloride	0.4–0.6 mg/kg/day	1	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
	Hydrochlorothiazide	0.5–1 mg/kg/day	1	3 mg/kg/day
	Triamteren	1–2 mg/kg/day	2	3–4 mg/kg/day up to 300 mg/day
Peripheral alpha-blockers	Doxazosin	1 mg/day	1	4 mg/day
	Prazosin	0.05–0.1 mg/kg/day	3	0.5 mg/kg/day
	Terazosin	1 mg/day	1	20 mg/day
Vasodilators	Hydralazine	0.75 mg/kg/dose	4	7.5 mg/kg/day up to 200 mg/day
	Minoxidil	0.2 mg/kg/dose	1–3	50–100 mg/day

Table XV. Selected causes of secondary hypertension in childhood

Kidney diseases	Glomerulonephritis Interstitial nephritis Cystic kidney disease Urinary tract defects Hydronephrosis Radiation-induced nephritis Renovascular diseases (including vasculitis) Renin-secreting tumour Obstructive (kidney stones, tumours, uretero-pelvic junction obstruction) Diabetic nephropathy Hypertension after kidney transplantation
Endocrine diseases	Primary hyperaldosteronism Mineralocorticoid metabolism disorders Congenital adrenal hyperplasia Cushing syndrome Pheochromocytoma Hyperparathyroidism Acromegaly Hyperthyroidism Hypothyroidism Carcinoid syndrome
Cardiovascular diseases	Coarctation of the aorta Aortic regurgitation Middle-aortic syndrome
Haematological diseases	Anaemia Policytaemia
Neurological diseases	Porphyria Vegetative neuropathy Increased intracranial pressure Subdural haematoma Tetraplegia Guillain-Barre syndrome Brain injury Brain tumour
Cancers	Wilms' tumour Mesoblastic nephroma Neuroblastoma CNS tumours
Acute stress	Burns Hypoglycaemia Hypoxia Perioperative period Psychogenic hyperventilation Abstinence in people addicted to alcohol and psychoactive substances
Induced by drugs and chemical agents, electrolyte disorders	mTOR inhibitors (cyclosporine, tacrolimus) Erythropoietin Oral contraceptives (oestrogens, progesterone) Glucocorticosteroids Mineralocorticoids Sympathomimetics

→

Table XV (cont.). Selected causes of secondary hypertension childhood

Induced by drugs and chemical agents, electrolyte disorders	MAO inhibitors Antidepressants (SSRI, TLPD) Buspiron Modafenil Carbamazepine Methylphenidate Non-steroidal anti-inflammatory drugs Vitamin D overdosing Hypercalcemia Theophylline Amphetamine and its derivates (ephedrine, pseudoephedrine) Cocaine Heroine Ginseng Heavy metals Anticancer drugs (anti-VGF antibodies, cisplatin, carboplatin, paclitaxel, docetaxel, 5-fluorouracil)
Gestational hypertension	Preeclampsia Eclampsia
Decreased vascular resistance	Arteriovenous fistulas Paget disease Beriberi
Hypervolaemia	Renal failure Heart failure SIADH
Obstructive sleep apnoea	Obesity Adenotonsillar hyperplasia Anatomic craniofacial defects
Syndromic hypertension	Syndromes: Turner Marfan Klinefelter Down Klippel-Trenaunay-Weber Feuerstein-Mims von Hippel-Lindau Recklinghausen Klippl-Feil Alagille Nodular sclerosis Ehlers-Danlos
Monogenic hypertension	Liddle Syndrome Apparent mineralocorticoid excess syndrome Psuedohypoaldosteronism type II MR mutation Familial hyperaldosteronism type I Familial hyperaldosteronism type III Steroid 17 alpha-hydroxylase deficiency Familial glucocorticoid resistance Hypertension with hypertension

Table XVI. Reference systolic blood pressure values (95th percentile) in neonates [126]

Age	Reference SBP values during the first year of life — 95th percentile [mmHg]	
	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

conditions and using the technique described in Table XVIII [129–135]. In neonates, infants and young children, auscultatory measurement is not recommended due to technical difficulties and a high prevalence of the white coat effect compared to automatic measurement. The BP measurement using the automatic oscillometric method is fraught with the risk of erroneous detection of elevated blood pressure values in the first measurement. In the case of indications for BP measurement in these age groups, if the result of the first measurement is incorrect, it is recommended to perform multiple consecutive measurements in short intervals (using automatic method).

The approach to the differential diagnosis of hypertension and the assessment of target organ damage in neonates does not differ from that in older age groups [135, 136] (Table XIX).

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 [137]. Initiation of pharmacological treatment is justified when BP values are above the 99th percentile, or target organ damage is present with BP values above the 95th percentile [138]. The general rule of pharmacological 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 XX). Oral antihypertensive therapy is reserved for neonates in a good overall clinical condition (Table XXI).

Table XVII. Blood pressure values at 2 weeks of life in neonates born between 26 and 44 weeks of gestation [127]

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

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

Early diagnostics of hypertension in post-hospital care in children born before 34 weeks of gestation

Prematurity and low birth weight are risk factors for developing hypertension. Estimates indicate that AH was diagnosed at the age of 3 in 7.3% of prematurely born children. The risk of developing AH increases with a younger gestational age and is particularly high in those born before 33 weeks of pregnancy.

Table XVIII. Technique of blood pressure measurements in neonates [130]

1. Measurement using an oscillometric device
2. 1.5 hours after feeding or a medical intervention
3. Child in lying position
4. Selection of an appropriately sized cuff
5. BP measurement on the right arm
6. Earlier placement of the cuff and BP measurement after 15 minutes of a quiet rest
7. BP measurement during sleep or in a quiet awake state
8. 3 properly performed BP measurements 1–2 minutes apart

Specialist post-hospital care of children born prematurely in whom blood pressure measurements are performed should be based on the principles outlined above and appropriate BP reference values should be used (see Neonatal hypertension).

Screening for hypertension in post-hospital care in children born prematurely (≤ 33 weeks of gestation)

These guidelines adopted the management principles published in 2018 by the Polish Neonatological Society and concerning post-hospital care for children born prematurely [5] as well as the Low Birth Weight and Nephron Number Working Group published in 2017 [139].

Children diagnosed with AH before discharge from the neonatal unit should be consulted and provided with specialist care in the paediatric hypertension centre during the hospitalization. Further diagnostic and therapeutic management should be based on the current paediatric guidelines of the Polish Society of Hypertension, the Children's Memorial Health Institute and the European Society of Hypertension.

Table XIX. Criteria for the diagnosis of target organ damage in neonates

Target organ damage parameters	Diagnostic criteria
Eye fundus	Grade 3/4 retinopathy according to Keith-Wagener-Barker classification
Microalbuminuria	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 ± 0.2 cm

Table XX. Intravenous antihypertensive drugs used in neonates

Antihypertensive drugs	Dosage	Comments
Diazoxide	2–5 mg/kg/dose Rapid intravenous infusion	Slow infusion is ineffective, it can cause rapid hypotension. Currently not used routinely in hypertension
Enalaprilat	15 ± 5 μg/kg/dose repeat every 8–24 h Injections every 5–10 minutes	May result in long-term hypotension or acute kidney failure Use limited due to these adverse effects
Esmolol	Infusion: 100–300 μg/kg/min	Short-acting drug, continuous infusion necessary
Hydralazine	Infusion: 0.75–5.0 μg/kg/min Bolus: 0.15–0.6 mg/kg/dose	Frequent tachycardia; boluses given every 4 hours
Labetalol	Infusion: 0.25–3.0 mg/kg/h Bolus: 0.2–1.0 mg/kg/dose	Contraindications: heart failure, bronchopulmonary dysplasia
Nicardipine	Infusion: 1–3 μg/kg/min	May result in reflex tachycardia
Sodium nitroprusside	Infusion: 0.5–10 μg/kg/min	Risk of cyanide poisoning if long-term use or renal failure

Table XXI. Oral antihypertensive drugs used in neonates

Antihypertensive drugs	Dosage	Mode of administration	Comments
Captopril	< 6 years: 0.01–0.5 mg/kg/dose Maximum 6 mg/kg/day	3 x/day	Drug of choice in most neonates Need to monitor potassium and creatinine level
Clonidine	2–5 μg/kg/dose Maximum 10 μg/kg/dose	2–3 x/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 x/day	Tachycardia and fluid retention are frequent adverse effects
Isradipine	0.05–0.15 mg/kg/dose Maximum 0.8 mg/kg/day	4 x/day	Effective in acute and chronic hypertension
Amlodipine	0.1–0.3 mg/kg/dose Maximum 0.6 mg/kg/day	2 x/day	Hypotension less frequent than with isradipine
Minoxidil	0.1–0.2 mg/kg/dose	2–3 x/day	The most potent oral vasodilating drug. Effective in resistant hypertension
Propranolol	0.5–1.0 mg/kg/ dose	3 x/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 x/day	Contraindicated in bronchopulmonary dysplasia Need to monitor heart rate
Spironolactone	0,5–1,5 mg/kg/dose	2 x/day	Results in potassium retention — need to monitor electrolytes Full effect seen after several days
Hydrochlorothiazide	1–3 mg/kg/dose	4 x/day	Need to monitor electrolytes
Chlorothazide	5–15 mg/kg/dose	2 x/day	Need to monitor electrolytes

Children with concomitant kidney and urinary tract pathology should be provided with specialist care in the nephrology, hypertension and paediatric urology centres. This will allow early planning of both treatment of urinary tract defect and renoprotective therapy.

In children in whom normal BP was detected discharge from the neonatal unit, BP should be measured at each medical visit. Automatic measurement on the right arm is recommended as the basic method of BP measurement In children younger than 3 years. If elevated blood pressure values are found, it should be confirmed by auscultatory measurement. The finding of hypertension is an indication to refer the child to the paediatric hypertensive centre.

References:

1. NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128•9 million children, adolescents, and adults. Lancet. 2017; 390(10113): 2627–2642, doi: 10.1016/S0140-6736(17)32129-3, indexed in Pubmed: 29029897.
2. Vuguin PM. Animal models for small for gestational age and fetal programming of adult disease. Horm Res. 2007; 68(3): 113–123, doi: 10.1159/000100545, indexed in Pubmed: 17351325.
3. Argente J, Mehls O, Barrios V. Growth and body composition in very young SGA children. Pediatr Nephrol. 2010; 25(4): 679–685, doi: 10.1007/s00467-009-1432-2, indexed in Pubmed: 20108001.
4. Tykarski A, Narkiewicz K, Gaciong Z, et al. 2015 Guidelines for the Management of Hypertension Part 1–7. Recommendations of the Polish Society of Hypertension. Arterial Hypertens. 2015; 19(2): 53–83, doi: 10.5603/AH.2015.0010.
5. Kit BK, Kuklina E, Carroll MD, et al. National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. Pediatrics. 2004; 114(2 Suppl 4th Report): 555–576, indexed in Pubmed: 15286277.
6. Baumgartner H, Bonhoeffer P, De Groot NM, et al. Task Force on the Management of Grown-up Congenital Heart Disease of the European Society of Cardiology (ESC); Association for European Paediatric Cardiology (AEPC); ESC Committee for Practice Guidelines (CPG). ESC Guidelines for the management of grown-up congenital heart disease (new version 2010). Eur Heart J. 2010; 31(23): 2915–2957, doi: 10.1093/eurheartj/ehq249, indexed in Pubmed: 20801927.
7. Urbina E, Alpert B, Flynn J, et al. American Heart Association Atherosclerosis, Hypertension, and Obesity in Youth Committee. Ambulatory blood pressure monitoring in children and adolescents: recommendations for standard assessment: a scientific statement from the American Heart Association Atherosclerosis, Hypertension, and Obesity in Youth Committee of the council on cardiovascular disease in the young and the council for high blood pressure research. Hypertension. 2008; 52(3): 433–451, doi: 10.1161/HYPERTENSIONAHA.108.190329, indexed in Pubmed: 18678786.
8. Standardy opieki ambulatoryjnej nad dzieckiem urodzonym przedwcześnie. Zalecenia Polskiego Towarzystwa Neonatologicznego i Polskiego Towarzystwa Pediatrycznego. Media Press 2017.

9. Kułaga Z, Litwin M, Grajda A, et al. OLAF Study Group. Oscillometric blood pressure percentiles for Polish normal-weight school-aged children and adolescents. J Hypertens. 2012; 30(10): 1942–1954, doi: 10.1097/HJH.0b013e328356abad, indexed in Pubmed: 22828086.
10. Symonides B, Jędrusik P, Artyszuk L, et al. Different diagnostic criteria significantly affect the rates of hypertension in 18-year-old high school students. Arch Med Sci. 2010; 6(5): 689–694, doi: 10.5114/aoms.2010.17082, indexed in Pubmed: 22419926.
11. Dereziński T, Kułaga Z, Litwin M. Prevalence of arterial hypertension and anthropometrical predictors of elevated blood pressure in 14 years old adolescents. Postępy Nauk Medycznych. 2015; 28(11): 756–759, doi: 10.5604/08606196.1190898.
12. Luyckx VA, Perico N, Somaschini M, et al. writing group of the Low Birth Weight and Nephron Number Working Group. A developmental approach to the prevention of hypertension and kidney disease: a report from the Low Birth Weight and Nephron Number Working Group. Lancet. 2017; 390(10092): 424–428, doi: 10.1016/S0140-6736(17)30576-7, indexed in Pubmed: 28284520.
13. Lurbe E, Cifkova R, Cruickshank JK, et al. Sociedad Europea de Hipertensión, European Society of Hypertension. Management of high blood pressure in children and adolescents: recommendations of the European Society of Hypertension. J Hypertens. 2009; 27(9): 1719–1742, doi: 10.1097/HJH.0b013e32832f4f6b, indexed in Pubmed: 19625970.
14. Rozporządzenie Ministra Zdrowia z dnia 29 sierpnia 2009 r. w sprawie świadczeń gwarantowanych z zakresu podstawowej opieki zdrowotnej Dz. U. 2009.139.1139.
15. Constantine E, Merritt C, Constantine E, et al. The assessment and management of hypertensive emergencies and urgencies in children. Pediatr Emerg Care. 2005; 21(6): 391–6; quiz 397, indexed in Pubmed: 15942520.
16. Flynn JT, Tullus K. Severe hypertension in children and adolescents: pathophysiology and treatment. Pediatr Nephrol. 2009; 24(6): 1101–1112, doi: 10.1007/s00467-008-1000-1, indexed in Pubmed: 18839219.
17. Flynn JT, Daniels SR, Hayman LL, et al. American Heart Association Atherosclerosis, Hypertension and Obesity in Youth Committee of the Council on Cardiovascular Disease in the Young. Update: ambulatory blood pressure monitoring in children and adolescents: a scientific statement from the American Heart Association. Hypertension. 2014; 63(5): 1116–1135, doi: 10.1161/HYP.0000000000000007, indexed in Pubmed: 24591341.
18. Kit BK, Kuklina E, Carroll MD, et al. National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. Pediatrics. 2004; 114(2 Suppl 4th Report): 555–576, indexed in Pubmed: 15286277.
19. Parati G, Stergiou GS, Asmar R, et al. ESH Working Group on Blood Pressure Monitoring. European Society of Hypertension guidelines for blood pressure monitoring at home: a summary report of the Second International Consensus Conference on Home Blood Pressure Monitoring. J Hypertens. 2008; 26(8): 1505–1526, doi: 10.1097/HJH.0b013e328308da66, indexed in Pubmed: 18622223.
20. Stergiou GS, Christodoulakis G, Giovas P, et al. Home blood pressure monitoring in children: how many measurements are needed? Am J Hypertens. 2008; 21(6): 633–638, doi: 10.1038/ajh.2008.38, indexed in Pubmed: 18443574.
21. Wright JT, Williamson JD, Whelton PK, et al. SPRINT Research Group. A Randomized Trial of Intensive versus Standard Blood-Pressure Control. N Engl J Med. 2015; 373(22): 2103–2116, doi: 10.1056/NEJMoa1511939, indexed in Pubmed: 26551272.
22. Atkins ER, Rodgers A, Xie X, et al. Effects of intensive blood pressure lowering on cardiovascular and renal outcomes: updated systematic review and meta-analysis. Lancet. 2016; 387(10017): 435–443, doi: 10.1016/S0140-6736(15)00805-3, indexed in Pubmed: 26559744.
23. Aatola H, Magnussen CG, Koivistoinen T, et al. Simplified definitions of elevated pediatric blood pressure and high adult arterial stiffness. Pediatrics. 2013; 132(1): e70–e76, doi: 10.1542/peds.2012-3426, indexed in Pubmed: 23753088.
24. Flynn JT, Kaelber DC, Baker-Smith CM, et al. Subcommittee On Screening And Management Of High Blood Pressure In Children. Clinical Practice Guideline for Screening and Management of High Blood Pressure in Children and Adolescents. Pediatrics. 2017; 140(3), doi: 10.1542/peds.2017-1904, indexed in Pubmed: 28827377.
25. Obrycki Ł, Litwin M. Nowe amerykańskie wytyczne postępowania w nadciśnieniu tętniczym u dzieci i młodzieży – najważniejsze zmiany wraz z komentarzem. Stand Med Ped. 2018; 15: 47–55.
26. Litwin M, Niemirska A, Sladowska-Kozlowska J, et al. Regression of target organ damage in children and adolescents with primary hypertension. Pediatr Nephrol. 2010; 25(12): 2489–2499, doi: 10.1007/s00467-010-1626-7, indexed in Pubmed: 20730452.
27. de Simone G, Daniels SR, Devereux RB, et al. Left ventricular mass and body size in normotensive children and adults: assessment of allometric relations and impact of overweight. J Am Coll Cardiol. 1992; 20(5): 1251–1260, indexed in Pubmed: 1401629.
28. Nagueh SF, Appleton CP, Gillebert TC, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography. J Am Soc Echocardiogr. 2009; 22(2): 107–133, doi: 10.1016/j.echo.2008.11.023, indexed in Pubmed: 19187853.
29. Litwin M, Niemirska A, Sladowska J, et al. Left ventricular hypertrophy and arterial wall thickening in children with essential hypertension. Pediatr Nephrol. 2006; 21(6): 811–819, doi: 10.1007/s00467-006-0068-8, indexed in Pubmed: 16565870.
30. Khoury PR, Mitsnefes M, Daniels SR, et al. Age-specific reference intervals for indexed left ventricular mass in children. J Am Soc Echocardiogr. 2009; 22(6): 709–714, doi: 10.1016/j.echo.2009.03.003, indexed in Pubmed: 19423289.
31. Dallaire F, Slorach C, Hui W, et al. Reference values for pulse wave Doppler and tissue Doppler imaging in pediatric echocardiography. Circ Cardiovasc Imaging. 2015; 8(2): e002167, doi: 10.1161/CIRCIMAGING.114.002167, indexed in Pubmed: 25632029.
32. de Simone G, Devereux RB, Daniels SR, et al. Effect of growth on variability of left ventricular mass: assessment of allometric signals in adults and children and their capacity to predict cardiovascular risk. J Am Coll Cardiol. 1995; 25(5): 1056–1062, indexed in Pubmed: 7897116.
33. Ong YT, Wong TY, Klein R, et al. Hypertensive retinopathy. N Engl J Med. 2004; 351(22): 2310–2317, doi: 10.1056/NEJMra032865, indexed in Pubmed: 15564546.
34. Dodson PM, Lip GY, Eames SM, et al. Hypertensive retinopathy: a review of existing classification systems and a suggestion for a simplified grading system. J Hum Hypertens. 1996; 10(2): 93–98, indexed in Pubmed: 8867562.
35. Feig DI, Johnson RJ. The role of uric acid in pediatric hypertension. J Ren Nutr. 2007; 17(1): 79–83, doi: 10.1053/j.jrn.2006.10.013, indexed in Pubmed: 17198939.
36. Loeffler LF, Navas-Acien A, Brady TM, et al. Uric acid level and elevated blood pressure in US adolescents: National Health and Nutrition Examination Survey, 1999-2006. Hypertension. 2012; 59(4): 811–817, doi: 10.1161/HYPERTENSIONAHA.111.183244, indexed in Pubmed: 22353609.
37. Reusz GS, Cseprekal O, Temmar M, et al. Reference values of pulse wave velocity in healthy children and teenagers. Hypertension. 2010; 56(2): 217–224, doi: 10.1161/HYPERTENSIONAHA.110.152686, indexed in Pubmed: 20566959.
38. Van Bortel LM, Laurent S, Boutouyrie P, et al. Artery Society, European Society of Hypertension Working Group on Vascular Structure and Function, European Network for Noninvasive Investigation of Large Arteries. Expert consensus document on the measurement of aortic stiffness in daily practice using carotid-femoral pulse wave velocity. J Hypertens. 2012; 30(3): 445–448, doi: 10.1097/HJH.0b013e32834fa8b0, indexed in Pubmed: 22278144.
39. Fischer DC, Schreiver C, Heimhalt M, et al. Pediatric reference values of carotid-femoral pulse wave velocity determined with an oscillometric device. J Hypertens. 2012; 30(11): 2159–2167, doi: 10.1097/HJH.0b013e3283582217, indexed in Pubmed: 22940681.

40. Jourdan C, Wühl E, Litwin M, et al. Normative values for intima-media thickness and distensibility of large arteries in healthy adolescents. J Hypertens. 2005; 23(9): 1707–1715, indexed in Pubmed: 16093916.
41. Litwin M, Niemirska A. Intima-media thickness measurements in children with cardiovascular risk factors. Pediatr Nephrol. 2009; 24(4): 707–719, doi: 10.1007/s00467-008-0962-3, indexed in Pubmed: 18784945.
42. Doyon A, Kracht D, Bayazit AK, et al. 4C Study Consortium. Carotid artery intima-media thickness and distensibility in children and adolescents: reference values and role of body dimensions. Hypertension. 2013; 62(3): 550–556, doi: 10.1161/HYPERTENSIONAHA.113.01297, indexed in Pubmed: 23817494.
43. Litwin M, Sladowska-Kozlowska K. Diagnostyka różnicowa nadciśnienia tętniczego u młodzieży. In: Litwin M, Prejbisz A, Januszewicz A. ed. Nadciśnienie tętnicze u młodzieży i młodych dorosłych. Medycyna Praktyczna 2011.
44. Wühl E, Trivelli A, Picca S, et al. ESCAPE Trial Group. Strict blood-pressure control and progression of renal failure in children. N Engl J Med. 2009; 361(17): 1639–1650, doi: 10.1056/NEJMoa0902066, indexed in Pubmed: 19846849.
45. Litwin M. Risk factors for renal failure in children with non-glomerular nephropathies. Pediatr Nephrol. 2004; 19(2): 178–186, doi: 10.1007/s00467-003-1329-4.
46. Litwin M, Grenda R, Sladowska J, et al. Add-on therapy with angiotensin II receptor 1 blocker in children with chronic kidney disease already treated with angiotensin-converting enzyme inhibitors. Pediatr Nephrol. 2006; 21(11): 1716–1722, doi: 10.1007/s00467-006-0223-2, indexed in Pubmed: 16909244.
47. Hadtstein C, Schaefer F. Hypertension in children with chronic kidney disease: pathophysiology and management. Pediatr Nephrol. 2008; 23(3): 363–371, doi: 10.1007/s00467-007-0643-7, indexed in Pubmed: 17990006.
48. Halbach SM, Martz K, Mattoo T, et al. Predictors of blood pressure and its control in pediatric patients receiving dialysis. J Pediatr. 2012; 160(4): 621–625.e1, doi: 10.1016/j.jpeds.2011.09.046, indexed in Pubmed: 22056352.
49. Kramer AM, van Stralen KJ, Jager KJ, et al. Demographics of blood pressure and hypertension in children on renal replacement therapy in Europe. Kidney Int. 2011; 80(10): 1092–1098, doi: 10.1038/ki.2011.232, indexed in Pubmed: 21814180.
50. Tkaczyk M, Nowicki M, Bałasz-Chmielewska I, et al. Hypertension in dialysed children: the prevalence and therapeutic approach in Poland--a nationwide survey. Nephrol Dial Transplant. 2006; 21(3): 736–742, doi: 10.1093/ndt/gfi280, indexed in Pubmed: 16303782.
51. Chavers BM, Solid CA, Daniels FX, et al. Hypertension in pediatric long-term hemodialysis patients in the United States. Clin J Am Soc Nephrol. 2009; 4(8): 1363–1369, doi: 10.2215/CJN.01440209, indexed in Pubmed: 19556378.
52. Chaudhuri A, Sutherland SM, Begin B, et al. Role of twenty-four-hour ambulatory blood pressure monitoring in children on dialysis. Clin J Am Soc Nephrol. 2011; 6(4): 870–876, doi: 10.2215/CJN.07960910, indexed in Pubmed: 21273374.
53. Inrig JK, Patel UD, Gillespie BS, et al. Relationship between interdialytic weight gain and blood pressure among prevalent hemodialysis patients. Am J Kidney Dis. 2007; 50(1): 108–18, 118.e1, doi: 10.1053/j.ajkd.2007.04.020, indexed in Pubmed: 17591530.
54. Charra B. Fluid balance, dry weight, and blood pressure in dialysis. Hemodial Int. 2007; 11(1): 21–31, doi: 10.1111/j.1542-4758.2007.00148.x, indexed in Pubmed: 17257351.
55. Paglialonga F, Ardissino G, Galli MA, et al. Bioimpedance analysis and cardiovascular status in pediatric patients on chronic hemodialysis. Hemodial Int. 2012; 16 Suppl 1: S20–S25, doi: 10.1111/j.1542-4758.2012.00743.x, indexed in Pubmed: 23036032.
56. Jain SR, Smith L, Brewer ED. Non-invasive intravascular monitoring in the pediatric hemodialysis population. Pediatr Nephrol. 2001; 16(1): 15–18, doi: 10.1007/s004670000504, indexed in Pubmed: 11198596.
57. Dietel T, Filler G, Grenda R, et al. Bioimpedance and inferior vena cava diameter for assessment of dialysis dry weight. Pediatr Nephrol. 2000; 14(10-11): 903–907, indexed in Pubmed: 10975296.
58. Laakkonen H, Happonen JM, Marttinen E, et al. Normal growth and intravascular volume status with good metabolic control during peritoneal dialysis in infancy. Pediatr Nephrol. 2010; 25(8): 1529–1538, doi: 10.1007/s00467-010-1535-9, indexed in Pubmed: 20446094.
59. Ortega LM, Materson BJ. Hypertension in peritoneal dialysis patients: epidemiology, pathogenesis, and treatment. J Am Soc Hypertens. 2011; 5(3): 128–136, doi: 10.1016/j.jash.2011.02.004, indexed in Pubmed: 21459067.
60. Levey AS, Rocco MV, Anderson S, et al. K/DOQI clinical practice guidelines on hypertension and antihypertensive agents in chronic kidney disease. Am J Kidney Dis. 2004; 43(5 Suppl 1): S1–S290., doi: 10.1053/j.ajkd.2004.03.003, indexed in Pubmed: 15114537.
61. Tentori F, Zhang J, Li Y, et al. Longer dialysis session length is associated with better intermediate outcomes and survival among patients on in-center three times per week hemodialysis: results from the Dialysis Outcomes and Practice Patterns Study (DOPPS). Nephrol Dial Transplant. 2012; 27(11): 4180–4188, doi: 10.1093/ndt/gfs021, indexed in Pubmed: 22431708.
62. Hoppe A, von Puttkamer C, Linke U, et al. A hospital-based intermittent nocturnal hemodialysis program for children and adolescents. J Pediatr. 2011; 158(1): 95–9, 99.e1, doi: 10.1016/j.jpeds.2010.06.036, indexed in Pubmed: 20691454.
63. Tan BK, Chan C, Davies SJ. Achieving euvolemia in peritoneal dialysis patients: a surprisingly difficult proposition. Semin Dial. 2010; 23(5): 456–461, doi: 10.1111/j.1525-139X.2010.00739.x, indexed in Pubmed: 21039874.
64. Wong H, Mylrea K, Feber J, et al. Prevalence of complications in children with chronic kidney disease according to KDOQI. Kidney Int. 2006; 70(3): 585–590, doi: 10.1038/sj.ki.5001608, indexed in Pubmed: 16788689.
65. Olin JW, Gornik HL, Bacharach JM, et al. Fibromuscular dysplasia: state of the science and critical unanswered questions: a scientific statement from the American Heart Association. Circulation. 2014; 129(9): 1048–1078, doi: 10.1161/01.cir.0000442577.96802.8c, indexed in Pubmed: 24548843.
66. Green R, Gu X, Kline-Rogers E, et al. Differences between the pediatric and adult presentation of fibromuscular dysplasia: results from the US Registry. Pediatr Nephrol. 2016; 31(4): 641–650, doi: 10.1007/s00467-015-3234-z, indexed in Pubmed: 26525198.
67. Slovut DP, Olin JW, Slovut DP, et al. Fibromuscular dysplasia. N Engl J Med. 2004; 350(18): 1862–1871, doi: 10.1056/NEJMra032393, indexed in Pubmed: 15115832.
68. Anderson WP, Kett MM, Stevenson KM, et al. Renovascular hypertension: structural changes in the renal vasculature. Hypertension. 2000; 36(4): 648–652, doi: 10.1161/01.hyp.36.4.648, indexed in Pubmed: 11040252.
69. Antoniewicz J, Litwin M, Pędich M, et al. Diagnosis and treatment of renovascular hypertension in children and adolescents — single center experience with 87 patients. J Hypertens. 2007; 25(suppl. 2): S332.
70. Trautmann A, Roebuck DJ, McLaren CA, et al. Non-invasive imaging cannot replace formal angiography in the diagnosis of renovascular hypertension. Pediatr Nephrol. 2017; 32(3): 495–502, doi: 10.1007/s00467-016-3501-7, indexed in Pubmed: 27747454.
71. Tullus K, Roebuck DJ, McLaren CA. Imaging in the evaluation of renovascular disease. Pediatr Nephrol. 2010; 25(6): 1049–1056, doi: 10.1007/s00467-009-1320-9, indexed in Pubmed: 19856000.
72. Shroff R, Roebuck DJ, Gordon I, et al. Angioplasty for renovascular hypertension in children: 20-year experience. Pediatrics. 2006; 118(1): 268–275, doi: 10.1542/peds.2005-2642, indexed in Pubmed: 16818574.
73. Kari JA, Roebuck DJ, McLaren CA, et al. Angioplasty for renovascular hypertension in 78 children. Arch Dis Child. 2015; 100(5): 474–478, doi: 10.1136/archdischild-2013-305886, indexed in Pubmed: 25527520.

74. Aggoun Y, Sidi D, Bonnet D. [Arterial dysfunction after treatment of coarctation of the aorta]. Arch Mal Coeur Vaiss. 2001; 94(8): 785–789, indexed in Pubmed: 11575204.
75. Bhat MA, Neelakandhan KS, Unnikrishnan M, et al. Fate of hypertension after repair of coarctation of the aorta in adults. Br J Surg. 2001; 88(4): 536–538, doi: 10.1046/j.1365-2168.2001.01745.x, indexed in Pubmed: 11298621.
76. Daniels SR. Repair of coarctation of the aorta and hypertension: does age matter. Lancet. 2001; 358(9276): 89–91, doi: 10.1016/S0140-6736(01)05378-8, indexed in Pubmed: 11463407.
77. O'Sullivan JJ, Derrick G, Darnell R. Prevalence of hypertension in children after early repair of coarctation of the aorta: a cohort study using casual and 24 hour blood pressure measurement. Heart. 2002; 88(2): 163–166, indexed in Pubmed: 12117846.
78. de Divitiis M, Pilla C, Kattenhorn M, et al. Ambulatory blood pressure, left ventricular mass, and conduit artery function late after successful repair of coarctation of the aorta. J Am Coll Cardiol. 2003; 41(12): 2259–2265, indexed in Pubmed: 12821257.
79. Brzezinska-Rajszys G, Qureshi SA, Ksiazyk J, et al. Middle aortic syndrome treated by stent implantation. Heart. 1999; 81(2): 166–170, doi: 10.1136/hrt.81.2.166, indexed in Pubmed: 9922353.
80. Adelman RD, Coppo R, Dillon MJ. The emergency management of severe hypertension. Pediatr Nephrol. 2000; 14(5): 422–427, indexed in Pubmed: 10805473.
81. Araki N, Umemura M, Miyagi Y, et al. Expression, transcription, and possible antagonistic interaction of the human Nedd4L gene variant: implications for essential hypertension. Hypertension. 2008; 51(3): 773–777, doi: 10.1161/HYPERTENSIONAHA.107.102061, indexed in Pubmed: 18268134.
82. Atanasov AG, Ignatova ID, Nashev LG, et al. Impaired protein stability of 11beta-hydroxysteroid dehydrogenase type 2: a novel mechanism of apparent mineralocorticoid excess. J Am Soc Nephrol. 2007; 18(4): 1262–1270, doi: 10.1681/ASN.2006111235, indexed in Pubmed: 17314322.
83. Bilginturan N, Zileli S, Karacadag S, et al. Hereditary brachydactyly associated with hypertension. J Med Genet. 1973; 10(3): 253–259, indexed in Pubmed: 4774535.
84. Botero-Velez M, Curtis JJ, Warnock DG. Brief report: Liddle's syndrome revisited--a disorder of sodium reabsorption in the distal tubule. N Engl J Med. 1994; 330(3): 178–181, doi: 10.1056/NEJM199401203300305, indexed in Pubmed: 8264740.
85. Li A, Tedde R, Krozowski ZS, et al. Molecular basis for hypertension in the "type II variant" of apparent mineralocorticoid excess. Am J Hum Genet. 1998; 63(2): 370–379, doi: 10.1086/301955, indexed in Pubmed: 9683587.
86. Toka O, Maass PG, Aydin A, et al. Childhood hypertension in autosomal-dominant hypertension with brachydactyly. Hypertension. 2010; 56(5): 988–994, doi: 10.1161/HYPERTENSIONAHA.110.156620, indexed in Pubmed: 20837885.
87. Vehaskari VM. Heritable forms of hypertension. Pediatr Nephrol. 2009; 24(10): 1929–1937, doi: 10.1007/s00467-007-0537-8, indexed in Pubmed: 17647025.
88. Stewart PM. Dexamethasone-suppressible hypertension. Lancet. 2000; 356(9231): 697–699, doi: 10.1016/s0140-6736(00)02624-6, indexed in Pubmed: 11085685.
89. Zimmet P, Alberti KG, Kaufman F, et al. IDF Consensus Group. The metabolic syndrome in children and adolescents - an IDF consensus report. Pediatr Diabetes. 2007; 8(5): 299–306, doi: 10.1111/j.1399-5448.2007.00271.x, indexed in Pubmed: 17850473.
90. Litwin M, Sladowska J, Syczewska M, et al. Metabolic abnormalities, insulin resistance, and metabolic syndrome in children with primary hypertension. Am J Hypertens. 2007; 20(8): 875–882, doi: 10.1016/j.amjhyper.2007.03.005, indexed in Pubmed: 17679036.
91. Litwin M, Niemirska A, Sladowska-Kozlowska J, et al. Regression of target organ damage in children and adolescents with primary hypertension. Pediatr Nephrol. 2010; 25(12): 2489–2499, doi: 10.1007/s00467-010-1626-7, indexed in Pubmed: 20730452.
92. Jarosz-Chobot P, Polanska J, Szadkowska A, et al. Rapid increase in the incidence of type 1 diabetes in Polish children from 1989 to 2004, and predictions for 2010 to 2025. Diabetologia. 2011; 54(3): 508–515, doi: 10.1007/s00125-010-1993-4, indexed in Pubmed: 21165594.
93. Fendler W, Borowiec M, Baranowska-Jazwiecka A, et al. Prevalence of monogenic diabetes amongst Polish children after a nationwide genetic screening campaign. Diabetologia. 2012; 55(10): 2631–2635, doi: 10.1007/s00125-012-2621-2, indexed in Pubmed: 22782286.
94. Margeirsdottir HD, Larsen JR, Brunborg C, et al. Norwegian Study Group for Childhood Diabetes. High prevalence of cardiovascular risk factors in children and adolescents with type 1 diabetes: a population-based study. Diabetologia. 2008; 51(4): 554–561, doi: 10.1007/s00125-007-0921-8, indexed in Pubmed: 18196217.
95. Rodriguez BL, Dabelea D, Liese AD, et al. SEARCH Study Group. Prevalence and correlates of elevated blood pressure in youth with diabetes mellitus: the SEARCH for diabetes in youth study. J Pediatr. 2010; 157(2): 245–251.e1, doi: 10.1016/j.jpeds.2010.02.021, indexed in Pubmed: 20394942.
96. Knerr I, Dost A, Lepler R, et al. Diabetes Data Acquisition System for Prospective Surveillance (DPV) Scientific Initiative Germany and Austria. Tracking and prediction of arterial blood pressure from childhood to young adulthood in 868 patients with type 1 diabetes: a multicenter longitudinal survey in Germany and Austria. Diabetes Care. 2008; 31(4): 726–727, doi: 10.2337/dc07-1392, indexed in Pubmed: 18184906.
97. Mayer-Davis EJ, Ma Bo, Lawson A, et al. SEARCH for Diabetes in Youth Study Group. Cardiovascular disease risk factors in youth with type 1 and type 2 diabetes: implications of a factor analysis of clustering. Metab Syndr Relat Disord. 2009; 7(2): 89–95, doi: 10.1089/met.2008.0046, indexed in Pubmed: 18847385.
98. Donaghue KC, Wadwa RP, Dimeglio LA, et al. International Society for Pediatric and Adolescent Diabetes. ISPAD Clinical Practice Consensus Guidelines 2014. Microvascular and macrovascular complications in children and adolescents. Pediatr Diabetes. 2014; 15 Suppl 20: 257–269, doi: 10.1111/pedi.12180, indexed in Pubmed: 25182318.
99. Maahs DM, Daniels SR, de Ferranti SD, et al. Cardiovascular disease risk factors in youth with diabetes mellitus: a scientific statement from the American Heart Association. Circulation. 2014; 130(17): 1532–1558, doi: 10.1161/CIR.0000000000000094, indexed in Pubmed: 25170098.
100. Afkarian M. Diabetic kidney disease in children and adolescents. Pediatr Nephrol. 2015; 30(1): 65–74; quiz 70, doi: 10.1007/s00467-014-2796-5, indexed in Pubmed: 24643739.
101. Pietrzak I, Mianowska B, Gadzicka A, et al. Blood pressure in children and adolescents with type 1 diabetes mellitus--the influence of body mass index and fat mass. Pediatr Endocrinol Diabetes Metab. 2009; 15(4): 240–245, indexed in Pubmed: 20455418.
102. Delaney A, Pellizzari M, Speiser PW, et al. Pitfalls in the measurement of the nocturnal blood pressure dip in adolescents with type 1 diabetes. Diabetes Care. 2009; 32(1): 165–168, doi: 10.2337/dc08-1319, indexed in Pubmed: 18984777.
103. Suláková T, Janda J, Cerná J, et al. Arterial HTN in children with T1DM--frequent and not easy to diagnose. Pediatr Diabetes. 2009; 10(7): 441–448, doi: 10.1111/j.1399-5448.2009.00514.x, indexed in Pubmed: 19500279.
104. Lurbe E, Redon J, Kesani A, et al. Increase in nocturnal blood pressure and progression to microalbuminuria in type 1 diabetes. N Engl J Med. 2002; 347(11): 797–805, doi: 10.1056/NEJMoa013410, indexed in Pubmed: 12226150.
105. Lucini D, Zuccotti G, Malacarne M, et al. Early progression of the autonomic dysfunction observed in pediatric type 1 diabetes mellitus. Hypertension. 2009; 54(5): 987–994, doi: 10.1161/HYPERTENSIONAHA.109.140103, indexed in Pubmed: 19805636.
106. Basiratnia M, Abadi SF, Amirhakimi GH, et al. Ambulatory blood pressure monitoring in children and adolescents with type-1 diabetes mellitus and its relation to diabetic control and microalbuminuria. Saudi J Kidney Dis Transpl. 2012; 23(2): 311–315, indexed in Pubmed: 22382225.
107. Basiratnia M, Abadi SF, Amirhakimi GH, et al. Ambulatory blood pressure monitoring in children and adolescents with type-1 diabetes mellitus and its relation to diabetic control and microalbuminuria. Saudi J Kidney Dis Transpl. 2012; 23(2): 311–315, indexed in Pubmed: 22382225.

108. Tołwińska J, Głowińska-Olszewska B, Bossowski A. Insulin therapy with personal insulin pumps and early angiopathy in children with type 1 diabetes mellitus. Mediators Inflamm. 2013; 2013: 791283, doi: 10.1155/2013/791283, indexed in Pubmed: 24347835.
109. Maahs DM, Daniels SR, de Ferranti SD, et al. Cardiovascular disease risk factors in youth with diabetes mellitus: a scientific statement from the American Heart Association. Circulation. 2014; 130(17): 1532–1558, doi: 10.1161/CIR.0000000000000094, indexed in Pubmed: 25170098.
110. Harrington J, Peña AS, Gent R, et al. Aortic intima media thickness is an early marker of atherosclerosis in children with type 1 diabetes mellitus. J Pediatr. 2010; 156(2): 237–241, doi: 10.1016/j.jpeds.2009.08.036, indexed in Pubmed: 19853860.
111. Fang ZY, Prins JB, Marwick TH. Diabetic cardiomyopathy: evidence, mechanisms, and therapeutic implications. Endocr Rev. 2004; 25(4): 543–567, doi: 10.1210/er.2003-0012, indexed in Pubmed: 15294881.
112. Kavey RE, Allada V, Daniels SR, et al. Cardiovascular risk reduction in high-risk pediatric patients: a scientific statement from the American Heart Association Expert Panel on Population and Prevention Science; the Councils on Cardiovascular Disease in the Young, Epidemiology and Prevention, Nutrition, Physical Activity and Metabolism, High Blood Pressure Research, Cardiovascular Nursing, and the Kidney in Heart Disease; and the Interdisciplinary Working Group on Quality of Care and Outcomes Research: endorsed by the American Academy of Pediatrics. Circulation. 2006; 114(24): 2710–2738, doi: 10.1161/CIRCULATIONAHA.106.179568, indexed in Pubmed: 17130340.
113. Afkarian M. Diabetic kidney disease in children and adolescents. Pediatr Nephrol. 2015; 30(1): 65–74; quiz 70, doi: 10.1007/s00467-014-2796-5, indexed in Pubmed: 24643739.
114. Salardi S, Balsamo C, Zucchini S, et al. High rate of regression from micro-macroalbuminuria to normoalbuminuria in children and adolescents with type 1 diabetes treated or not with enalapril: the influence of HDL cholesterol. Diabetes Care. 2011; 34(2): 424–429, doi: 10.2337/dc10-1177, indexed in Pubmed: 21216861.
115. Rodriguez BL, Dabelea D, Liese AD, et al. SEARCH Study Group. Prevalence and correlates of elevated blood pressure in youth with diabetes mellitus: the SEARCH for diabetes in youth study. J Pediatr. 2010; 157(2): 245–251.e1, doi: 10.1016/j.jpeds.2010.02.021, indexed in Pubmed: 20394942.
116. TODAY Study Group. Rapid rise in hypertension and nephropathy in youth with type 2 diabetes: the TODAY clinical trial. Diabetes Care. 2013; 36(6): 1735–1741, doi: 10.2337/dc12-2420, indexed in Pubmed: 23704672.
117. TODAY Study Group. Lipid and inflammatory cardiovascular risk worsens over 3 years in youth with type 2 diabetes: the TODAY clinical trial. Diabetes Care. 2013; 36(6): 1758–1764, doi: 10.2337/dc12-2388, indexed in Pubmed: 23704675.
118. Springer SC, Silverstein J, Copeland K, et al. American Academy of Pediatrics. Management of type 2 diabetes mellitus in children and adolescents. Pediatrics. 2013; 131(2): e648–e664, doi: 10.1542/peds.2012-3496, indexed in Pubmed: 23359584.
119. 2015 Guidelines on the management of diabetic patients. A position of Diabetes Poland. Clin Diabetol. 2015; 4(Suppl. A): A41–A47.
120. Maahs DM, Daniels SR, de Ferranti SD, et al. Cardiovascular disease risk factors in youth with diabetes mellitus: a scientific statement from the American Heart Association. Circulation. 2014; 130(17): 1532–1558, doi: 10.1161/CIR.0000000000000094, indexed in Pubmed: 25170098.
121. American Diabetes Association. Standards of medical care in diabetes —2014. Diabetes Care. 2014; 37 (Suppl 1): S14–S80, doi: 10.2337/dc14-S014, indexed in Pubmed: 24357209.
122. Chatterjee M, Speiser PW, Pellizzarri M, et al. Poor glycemic control is associated with abnormal changes in 24-hour ambulatory blood pressure in children and adolescents with type 1 diabetes mellitus. J Pediatr Endocrinol Metab. 2009; 22(11): 1061–1067, indexed in Pubmed: 20101892.
123. Bullo M, Tschumi S, Bucher BS, et al. Pregnancy outcome following exposure to angiotensin-converting enzyme inhibitors or angiotensin receptor antagonists: a systematic review. Hypertension. 2012; 60(2): 444–450, doi: 10.1161/HYPERTENSIONAHA.112.196352, indexed in Pubmed: 22753220.
124. Constantine E, Merritt C, Constantine E, et al. The assessment and management of hypertensive emergencies and urgencies in children. Pediatr Emerg Care. 2005; 21(6): 391–6; quiz 397, indexed in Pubmed: 15942520.
125. Task Force on Blood Pressure Control in Children. Report of the Second Task Force on Blood Pressure Control in Children — 1987. Pediatrics. 1987; 79(1): 1–25.
126. Skalina ME, Kliegman RM, Fanaroff AA. Epidemiology and management of severe symptomatic neonatal hypertension. Am J Perinatol. 1986; 3(3): 235–239, doi: 10.1055/s-2007-999874, indexed in Pubmed: 3718646.
127. Friedman AL, Hustead VA. Hypertension in babies following discharge from a neonatal intensive care unit. A 3-year follow-up. Pediatr Nephrol. 1987; 1(1): 30–34, indexed in Pubmed: 3153257.
128. Buchi KF, Siegler RL. Hypertension in the first month of life. J Hypertens. 1986; 4(5): 525–528, indexed in Pubmed: 3794327.
129. Dionne JM, Abitbol CL, Flynn JT. Hypertension in infancy: diagnosis, management and outcome. Pediatr Nephrol. 2012; 27(1): 17–32, doi: 10.1007/s00467-010-1755-z, indexed in Pubmed: 21258818.
130. Low JA, Panagiotopoulos C, Smith JT, et al. Validity of newborn oscillometric blood pressure. Clin Invest Med. 1995; 18(3): 163–167, indexed in Pubmed: 7554582.
131. Langbaum M, Eyal FG. A practical and reliable method of measuring blood pressure in the neonate by pulse oximetry. J Pediatr. 1994; 125(4): 591–595, indexed in Pubmed: 7931880.
132. Nwankwo MU, Lorenz JM, Gardiner JC. A standard protocol for blood pressure measurement in the newborn. Pediatrics. 1997; 99(6): E10, indexed in Pubmed: 9164806.
133. Park MK, Menard SM. Normative oscillometric blood pressure values in the first 5 years in an office setting. Am J Dis Child. 1989; 143(7): 860–864, indexed in Pubmed: 2741863.
134. Park MK, Menard SW, Yuan C. Comparison of auscultatory and oscillometric blood pressures. Arch Pediatr Adolesc Med. 2001; 155(1): 50–53, indexed in Pubmed: 11177062.
135. O'Brien E, Mee F, Atkins N, et al. Evaluation of three devices for self-measurement of blood pressure according to the revised British Hypertension Society Protocol: the Omron HEM-705CP, Philips HP5332, and Nissei DS-175. Blood Press Monit. 1996; 1(1): 55–61, indexed in Pubmed: 10226203.
136. Peterson AL, Frommelt PC, Mussatto K. Presentation and echocardiographic markers of neonatal hypertensive cardiomyopathy. Pediatrics. 2006; 118(3): e782–e785, doi: 10.1542/peds.2006-0631, indexed in Pubmed: 16880252.
137. Watkinson M. Hypertension in the newborn baby. Arch Dis Child Fetal Neonatal Ed. 2002; 86(2): F78–F81, indexed in Pubmed: 11882547.
138. Feld LG, Waz WR. Pharmacologic therapy of hypertension. In: Feld LG. ed. Hypertension in Children. Butterworth-Heinemann, Boston 1997: 133–178.
139. Luyckx VA, Perico N, Somaschini M, et al. writing group of the Low Birth Weight and Nephron Number Working Group. A developmental approach to the prevention of hypertension and kidney disease: a report from the Low Birth Weight and Nephron Number Working Group. Lancet. 2017; 390(10092): 424–428, doi: 10.1016/S0140-6736(17)30576-7, indexed in Pubmed: 28284520.