Polish Society of Hypertension

2019 Guidelines for the Management of Hypertension

Part 1–7

Recommendations of the Polish Society of Hypertension

Guideline editors: Andrzej Tykarski, Krzysztof J. Filipiak, Andrzej Januszewicz, Mieczysław Litwin, Krzysztof Narkiewicz, Aleksander Prejbisz, Danuta Ostalska-Nowicka, Krystyna Widecka, Katarzyna Kostka-Jeziorny

Experts: Marcin Adamczak, Marta Buraczewska, Ludwina Szczepaniak-Chicheł, Marzena Chrostowska, Danuta Czarnecka, Piotr Dobrowolski, Grzegorz Dzida, Zbigniew Gaciong, Jerzy Gąsowski, Tomasz Grodzicki, Dagmara Hering, Beata Wożakowska-Kapłon, Przemysław Kosiński, Beata Begier-Krasińska, Jan Krekora, Jacek Manitius, Małgorzata Myśliwiec, Anna Niemirska, Arkadiusz Niklas, Łukasz Obrycki, Agnieszka Olszanecka, Sylwester Prokurat, Grażyna Brzezińska-Rajszys, Marek Rajzer, Katarzyna Stolarz-Skrzypek, Agnieszka Szadkowska, Filip M. Szymański, Anna Szyndler, Andrzej Więcek, Barbara Wizner, Jacek Wolf, Tomasz Zdrojewski

Arterial Hypertens. 2019, vol. 23, no. 2, pages: 41–87
DOI: 10.5603/AH.a2019.0008

Introduction

The Polish Society of Hypertension (PTNT) presents a new edition — fifth over the last 16 years — of its guidelines for the management of hypertension, the most common disease in Poland.

During four years that have passed since publication of the previous 2015 guidelines, results of multiple important studies and metaanalyses evaluating antihypertensive therapy have been published. These results have extended the range of available information, leading to modification of some concepts in the management of hypertension, in particular regarding optimal target blood pressure values, treatment intensity, strategies to improve adherence, approach to the treatment of resistant and secondary hypertension, including interventional treatment, and non-blood pressure lowering therapy to reduce cardiovascular risk.

The present document is generally based on the 2015 PTNT guidelines, retaining its practical nature with consideration of specific aspects of the diagnosis and drug treatment of hypertension in Poland, but it also includes some new teaching concepts and most of the changes, which were considered appropriate by the authors of the present guidelines, that were introduced in the most recent 2018 European Society of Cardiology/European Society of Hypertension (ESC/ESH) guidelines.

Instead of typical recommendation grading (including classes of recommendations and levels of evidence), a traffic light signalling system-based classification has been retained in the tables summarising the basic principles of the management of hypertension, reflecting not only available evidence but also expert opinion to a greater degree compared to the 2018 ESC/ESH guidelines.

These colours mean:

green — a given management approach is recommended, generally based on clear evidence from research studies, or unequivocal expert opinion reflecting current clinical practice

yellow — a given management approach is suggested as appropriate despite weaker supporting data due to lacking or equivocal evidence from research studies, based on the opinion of the majority of experts reflecting common sense and their personal clinical experience

red — a given management approach should be abandoned as it is considered not justified or harmful, generally based on clear evidence from research studies or the opinion of the majority of experts

1. Epidemiology and prevention of hypertension

Hypertension remains the most important modifiable cardiovascular risk factor, and according to the World Health Organisation, it is also most common cause of premature mortality worldwide. Blood pressure (BP) values show a linear correlation with mortality and the incidence of cardiovascular disease (myocardial infarction, stroke, peripheral arterial disease) and chronic kidney disease in all age and ethnic groups in both women and men. Among subjects above 50 years of age, systolic blood pressure (SBP) is a better indicator of cardiovascular risk, and pulse pressure or the difference between SBP and diastolic blood pressure (DBP) is an additional marker of an increased risk.

Data obtained during the last 20 years indicate an increasing prevalence of hypertension in Poland. The NATPOL 2011 study showed that over 10 years, the prevalence of hypertension in individuals aged 18–79 years increased from 30% to 32% or 9.5 million people, based on BP measurements during two separate visits. In addition, the POLSENIOR study indicates that hypertension is present in more than one million of people above 80 years of age. In the 2014 WOBASZ II study, the prevalence of elevated BP values in adult Poles aged 19–99 years was 42.7%. The proportion of subjects with a previous diagnosis of hypertension was 59.3%, treatment was initiated in 46.1%, and BP was controlled in 23%. Considering that prevalence estimates are at least 9% lower when the diagnosis of hypertension is based on BP measurements during at least two separate visits, as recommended in the guidelines, compared to those during a single visit, the number of subjects with hypertension in Poland based on the NATPOL and WOBASZ studies can be estimated at about 11 million. If these trends continue, it has been estimated that the number of subjects with hypertension in Poland will have increased by half until 2035.

Development of hypertension may be best prevented by interventions targeted at environmental factors. The most effective approach to prevent or delay development of hypertension (primary prevention) is lifestyle modification, in particular preventing obesity and increasing physical activity. Primary prevention may be divided into population efforts, directed at the general population, and prevention targeted at those at an increased risk of hypertension. The latter, more intensive efforts should focus on the following groups:

1. Subjects with a family history of premature cardiovascular disease (stroke, myocardial infarction, heart failure) — below 65 years of age in women and 55 years of age in men.
2. Patients with diabetes or concomitant kidney disease.
3. Subjects with at least two conventional cardiovascular risk factors.
4. Subjects with BP ≥130/85 mm Hg.

The goal of primary prevention is to increase detection of hypertension, possibly in its early asymptomatic period when target organ damage is still absent or limited. Preventive efforts should also be targeted at those with established hypertension. About 30% of subjects are unaware of hypertension which results from the fact that nearly 40% of people in Poland do not know their BP values. Due to low hypertension detection rate in Poland, screening BP measurements are recommended in all adults at least once a year regardless of previous BP values.

Late secondary (tertiary) prevention includes therapeutic interventions in subjects with established disease to prevent or at least delay adverse sequelae of hypertension (cardiovascular and renal complications). Public awareness of the risks associated with high BP has increased but remains unsatisfactory. The NATPOL 2011 study showed that the proportion of subjects with the diagnosis of hypertension who remained untreated decreased from 18% to 13%.

2. Diagnosis and classification

The diagnosis of hypertension is based on properly performed office BP measurements. Due to the ban on the use of mercury in the European Union, semiautomatic auscultatory or oscillometric sphygmomanometers are currently recommended for BP measurements. Obtaining reliable BP value requires use of an adequately accurate device, appropriate patient preparation, and proper measurement technique (Tab. I). Brachial BP measurements using certified BP measurement devices are recommended (the list of certified BP measurement devices may be found at the Polish Society of Hypertension [Polskie Towarzystwo Nadciśnienia Tętniczego, PTNT] website at www.nadcisnienietetnicze.pl/dla_lekarzy/zalecenia_i_standardy/zalecenia_ptnt).

Hypertension may be diagnosed if average BP values (calculated based on **at least two** measurements on at least two different visits) are equal to or higher than **140 mm Hg** (SBP) and/or **90 mm Hg** (DBP).

In patients with SBP values 140–159 mm Hg and DBP values 90–99 mm Hg at low to moderate cardiovascular risk, the diagnosis of hyperten-

Table I. Principles and proper technique of office blood pressure measurements

Equipment requirements
Validated device with an arm cuff (see www.nadcisnienietetnicze.pl/dla_lekarzy/zalecenia_i_standardy/zalecenia_ptnt)
In most patients, BP measurement should be performed using a standard size arm cuff (width 12–13 cm, length 35 cm); a larger cuff should be used with the patient's arm circumference > 32 cm, and a smaller cuff with arm circumference < 24 cm
Patient preparation
Patients should refrain from drinking coffee, smoking cigarettes, and using other stimulants for at least 30 minutes before the measurement
Measurement should be performed after at least 5 minutes of rest, in a sitting position with the back supported, in a quiet room at comfortable ambient temperature. The arm on which BP is measured should be flexed at the elbow and loosely supported at the level of the heart. The upper arm should be free from any restrictive clothing
Measurement technique
When measuring using the classical (auscultatory) technique, the cuff should be inflated to 30 mm Hg above the audible sounds (palpable pulse). The cuff should be deflated at a rate of 2 mm Hg/s
Initially, BP should be measured on both arms, with further measurements on the arm with the higher BP reading for long-term BP monitoring and evaluation of the effectiveness of antihypertensive therapy
With the auscultatory technique, systolic blood pressure (SBP) is defined as the appearance of the first tone during cuff deflation — Korotkoff phase I, and diastolic blood pressure (DBP) is defined as the disappearance of the last tone during cuff deflation — Korotkoff phase V
BP should be calculated as the mean of 2 last measurements, the standard being at least 3 BP measurements performed 1–2 minutes apart during the same visit. If BP values differ between subsequent measurements (> 10 mm Hg), additional measurements should be performed
BP measurements in patients with arrhythmia (e.g., atrial fibrillation) should be performed using the auscultatory technique
At the initial evaluation, orthostatic challenge (active standing) test should be performed in all patients, with BP measurements at 1 and 3 minutes after standing up from the sitting position. Orthostatic hypotension is defined as SBP fall by ≥ 20 mm Hg or to < 90 mm Hg or DBP fall by ≥ 10 mm Hg. Active lying-to-standing test (standing up from the lying position) should be considered in the elderly, diabetic patients, and patients with other conditions associated with an increased risk of orthostatic hypotension. Extending orthostatic BP measurements to 5 minutes should be considered in these groups
Pulse rate should be measured to exclude significant arrhythmia. Resting heart rate is also used for cardiovascular risk evaluation
If a BP difference is found between the arms, the higher value should be taken as actual BP (preferred simultaneous BP measurement, and if not available — sequential BP measurement)

BP — blood pressure; DBP — diastolic blood pressure; SBP — systolic blood pressure

sion should be confirmed, if possible, by ambulatory blood pressure monitoring (ABPM) or by home BP measurements (Tab. II), using different threshold values (Tab. III).

In patients with SBP values ≥ 180 mm Hg and/or DBP values ≥ 110 mm Hg, the diagnosis of hypertension may be made at the first visit after excluding an effect of factors leading to acute BP elevation, e.g., anxiety, pain, or alcohol intake.

The diagnosis of hypertension may also be made based on data from the history or patient medical records [BP values or use of antihypertensive medications, presence of hypertension-mediated organ damage (HMOD)].

The classification of hypertension is based on office BP measurements, with three grades of severity and the separate subtype of isolated systolic hypertension (ISH). Detailed classification of hypertension is shown in Table IV.

Blood pressure values are of major importance when stratifying cardiovascular risk of the patient.

2.1. Automated office blood pressure measurements

The technique of automated office BP measurements (AOBPM) is similar to that of conventional office BP measurements, the difference being the absence of medical personnel with the patient during serial measurements. The device is programmed to perform serial BP measurements 1–3 minutes apart, starting with a 5 minute delay, after the nurse of the physician leaves the examination room. This approach allows to reduce or eliminate the effect of stress on BP values (white coat effect). BP values obtained during AOBPM are usually lower compared to conventional office BP measurements (SBP by about 5–15 mm Hg) and comparable to home and ambulatory BP measurements during activity. Due to very limited data regarding prediction of cardiovascular events based on AOBPM, unclear relation to office BP values, and low use of the method, normal values and diagnostic thresholds have not been defined yet for this BP measurement approach.

Table II. Recommendations regarding home blood pressure measurements

Fully automated devices with an arm cuff are recommended (see www.nadcisnienietetnicze.pl/dla_lekarzy/zalecenia_i_standardy/zalecenia_ptnt)
Measurements should be performed during 6-7 subsequent days before the visit (minimum 3 days)
Two BP measurements should be performed several minutes apart in the morning and in the evening, at constant times of the day (e.g., 6.00 AM–6.00 PM, 7.00 AM–7.00 PM). Measurements should be performed before drug intake and before meals
Measurements should be performed according to the principles described in Table I
The patient should record BP values measured in a diary
For calculation of the mean BP for HBPM, values obtained during the first day should be discarded
Purposefulness of HBPM should be considered in patients with an elevated level of anxiety
Home BP values should not be used for self-modifications of the therapy by the patient

BP — blood pressure; HBPM — home blood pressure monitoring

Table III. Diagnosis of hypertension based on office and out-of-office blood pressure measurements

Category	SBP [mm Hg]		DBP [mm Hg]
Office BP measurements	≥ 140	and/or	≥ 90
Ambulatory BP measurements			
— daytime (or awake) mean	≥ 135	and/or	≥ 85
— night-time (or sleep) mean	≥ 120	and/or	≥ 70
— mean 24-hour	≥ 130	and/or	≥ 80
Home BP measurements (mean from at least 3 days)	≥ 135	and/or	≥ 85

P — blood pressure; DBP — diastolic blood pressure; SBP — systolic blood pressure

Table IV. Definitions and classification of office blood pressure levels. Grades of hypertension apply only to office blood pressure measurements

Category	SBP [mm Hg]		DBP [mm Hg]
Optimal BP	< 120	and	< 80
Normal BP	120–129	and/or	80–84
High normal BP	130–139	and/or	85–89
Grade 1 hypertension	140–149	and/or	90–99
Grade 2 hypertension	160–179	and/or	100–109
Grade 3 hypertension	≥ 180	and/or	≥ 110
Isolated systolic hypertension	≥ 140	and	< 90

BP — blood pressure; DBP — diastolic blood pressure; SBP — systolic blood pressure

2.2. Out-of-office blood pressure measurements

Out-of-office BP measurements are used for the diagnosis of hypertension and to monitor the effects of antihypertensive therapy. Information obtained from ABPM and home BP measurements (HBPM) should be considered complementary. By comparing office and out-of-office BP measurements, it is possible to define phenotypes that cannot be identified based on conventional office BP measurements only (i.e., white coat hypertension, white coat effect, masked hypertension, or masked uncontrolled hypertension).

2.2.1 Home blood pressure measurements

Home BP measurements not only reduce the risk of a white-coat effect, often observed during office BP measurements, but also show good agreement with daytime ABPM measurements. In addition, home BP values correlate with cardiovascular risk better than office BP values. In the diagnosis of hypertension abnormal home BP values are defined as the average of several measurements greater than or equal to 135 and/or 85 mm Hg.

Daily home BP measurements should be advised particularly during the week prior to a follow-up

visit, serving as a basis for medication adjustments by a physician.

Blood pressure self-measurement is relatively easy for the patient and may contribute to improved compliance and treatment effectiveness by engaging the patient in the therapeutic process. Prerequisites include teaching the patient proper measurement technique and use of a validated device. Difficulties may arise from the fact that only some devices available on the Polish market fulfil the quality criteria.

Specific indications for HBPM are listed in Table II.

2.2.2. Ambulatory blood pressure monitoring

Ambulatory blood pressure monitoring is usually undertaken for 24 hours (less frequently for 2 days). Measurement intervals are set at 15–30 minutes during activity and 30–60 minutes during sleep. Increasing the number of BP measurements performed out-of-office, in conditions that reflect the usual patient environment, allows more reliable evaluation of actual BP values. Normal BP by ABPM is defined as mean daytime values below 135/85 mm Hg, mean night-time values below 120/70 mm Hg, and mean 24-hour values below 130/80 mm Hg. Mean BP values obtained by ABPM (or HBPM) better reflect the risk of cardiovascular events and correlate more strongly with the presence of target organ damage compared to office BP values.

Despite clear clinical utility, ABPM also has some limitations including high cost, still suboptimal availability, and unclear reproducibility (though the latter is higher compared to office BP measurements). To obtain reliable measurements, it is necessary to use validated devices and a standardised measurement technique.

ABPM allows detection of prognostically adverse phenomena including white coat effect, excessive morning BP surge, and non-dipper, extreme-dipper, and reverse-dipper patterns of the circadian BP rhythm. A very important indication for ABPM is verification of the diagnosis of hypertension, particularly in patients with grade 1 hypertension by office BP measurements. Specific indications for ABPM are listed in Table V.

3. Investigations

At the time of the diagnosis of hypertension, all patients should undergo comprehensive clinical evaluation that includes targeted history, physical examination, and selected laboratory tests and other investigations as required.

The goals of clinical evaluation include identification of:

1. The cause of elevated BP and indications for investigating for possible secondary hypertension.
2. Target organ damage and the presence and severity of other diseases, including cardiovascular and kidney disease.
3. Concomitant diabetes and its complications.
4. Other concomitant cardiovascular risk factors.

3.1. Patient history

Important issues to consider during history taking should include duration of hypertension, previously observed BP values, and previous treatment and its effects. Information should be obtained regarding possible evidence of secondary hypertension, presence of risk factors and concomitant diseases, and the family history of hypertension, cardiovascular disease, and kidney disease that might indicate a hereditary background. Other medications taken by the patient that might affect BP values should be noted, along with possible evidence of noncompliance (the patient does not know names and doses of the medications, irregular visits, missing medical records, large variability of home BP values). In women, BP values during pregnancy should be ascertained. History should also be taken regarding substance use, including alcohol intake and tobacco smoking (quantified by the number of pack-years), changes in body weight, and dietary habits.

3.2. Physical examination

Complete physical examination should be performed in all patients, taking particular note of findings indicating secondary hypertension and the presence of target organ damage.

Patient body weight and height should be documented, along with calculation of the body mass index (BMI), defined as body weight in kilograms divided by squared height in metres. Overweight is defined as BMI ≥ 25 kg/m^2, and obesity as BMI ≥ 30 kg/m^2. Due to the fact that interpretation of BMI values may be challenging in some patient groups (e.g., in the elderly), waist circumference should also be evaluated by measuring waist circumference (in a horizontal plane at the superior aspect of the iliac crest) to identify abdominal obesity. In clinical practice, waist circumference > 80 cm in women and > 94 cm in men should be considered alerting, and waist circumference > 88 cm in women and > 102 cm in men should be considered critical and clearly requiring weight reduction.

Table V. Indications for and technique of ambulatory blood pressure measurements

Indications for ABPM
Confirmation of the diagnosis of hypertension in patients with grade 1 hypertension by office BP measurements and low/moderate cardiovascular risk
Suspicion of white-coat hypertension — grade 1 hypertension by office BP measurements — hypertension without target organ damage and with low global cardiovascular risk — large BP differences in office measurements (> 20 mm Hg) or differences between home and office readings
Suspicion of masked hypertension — high normal BP by office measurements — normal office BP readings in individuals with subclinical target organ damage or high global cardiovascular risk — suspicion of nocturnal hypertension and/or abnormal 24-hour BP pattern
Suspicion of hypotension (dizziness, falls, presyncope, syncope) or autonomic system dysfunction
Identification of true resistant or pseudo resistant hypertension — suspicion of white-coat effect in treated hypertensives
Hypertension in pregnant women
Specific indications for ABPM — hypertension in patients with glaucoma — assessment of nocturnal BP values and fall in patients with obstructive sleep apnoea, diabetes, chronic kidney disease or after vascularized organ transplantation
Technique of ABPM
First, measure BP on both arms with a conventional sphygmomanometer according to the general principles (see Tab. I)
Depending on BP difference between arms: ≤ 10 mm Hg (SBP) — place the cuff on the non-dominant arm > 10 mm Hg — place the cuff on the arm with higher BP reading
Choose an appropriately-sized cuff and measure BP using the automated device
If the difference between initial BP reading and BP read by the automated device is greater than 5 mm Hg, re-adjust the cuff
Set BP measurement intervals (preferred intervals 15–20 minutes during the day and 30 minutes during the night)
Switch off BP reading display
Provide the patient with a diary to record activity during the monitoring (along with a contact phone number)
A recording is acceptable if it includes at least 70% of the planned BP readings during the day and night

ABPM — ambulatory blood pressure monitoring; BP — blood pressure; SBP — systolic blood pressure

3.3. Laboratory investigations

Laboratory investigations recommended in patients with hypertension may be categorised into:

1. **Routine tests** — necessary in all patients with hypertension.
2. **Additional tests** — performed in all patients if available.
3. **Extended tests** — performed in some patients during more extensive diagnostic work-up in reference centres.

3.3.1. Routine tests

Routine tests include:

- full blood count;
- fasting blood glucose level or oral glucose tolerance test (OGTT) if indicated;
- serum sodium and potassium level;
- total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, and triglyceride levels;
- serum creatinine level with estimated glomerular filtration rate (eGFR);
- serum uric acid level;
- serum thyroid-stimulating hormone (TSH) level;
- serum alanine aminotransferase (ALT) activity;
- urinalysis (with urine sediment examination);
- evaluation of albuminuria (by dipstick test or other method);
- 12-lead electrocardiogram (ECG).

Based on these routine tests, it is possible to obtain information regarding the presence of HMOD, such as left ventricular hypertrophy (ECG), arterial stiffness (BP measurement, yielding pulse pressure

as SBP minus DBP), and kidney damage (serum creatinine and eGFR, urinalysis with urine sediment examination).

3.3.2. Additional tests

For more complete evaluation of HMOD and cardiovascular risk and screening for secondary hypertension, additional tests to be performed in all patients with hypertension, if available, include:

- renal ultrasound with renal artery Doppler examination;
- echocardiography*;
- urinary albumin-to-creatinine ratio (UACR) (in morning urine sample);
- aldosterone-to-renin ratio (ARR) after 2 hours in upright position (patients with grade 2 and 3 hypertension);
- fundoscopy (patients with grade 2 and 3 hypertension).

In all women of childbearing age with hypertension, qualitative evaluation of proteinuria and renal ultrasound with renal artery Doppler examination should be performed. Quantitative evaluation of proteinuria should be considered in all women planning pregnancy.

*Compared to ECG, echocardiography is more sensitive at detecting left ventricular hypertrophy and it provides important information regarding cardiac structure and function. It allows more precise evaluation of the cardiovascular risk and is useful for monitoring treatment effectiveness during long-term follow-up. Echocardiographic examination should include evaluation of:

- left ventricular mass and interventricular septum and posterior wall thickness;
- left ventricular systolic function;
- left ventricular diastolic function (with particular consideration of left atrial size);
- presence of aortic dilatation and evidence of coarctation of the aorta;
- cardiac valves.

3.3.3 Extended tests

Depending on indications, investigations in patients with hypertension may be extended to include:

- carotid artery ultrasound;
- 24-hour ECG monitoring if arrhythmia is present;
- ankle-brachial index (ABI);
- pulse wave velocity (PWV);
- 24-hour urinary sodium and potassium excretion;
- quantitative evaluation of proteinuria/albuminuria.

Further specialised tests are used to identify some forms of target organ damage (e.g., magnetic resonance imaging in subjects with suspected hypertensive encephalopathy) and are usually necessary to confirm or exclude secondary hypertension. A sum-

Table VI. Routine, additional, and extended laboratory investigations in hypertensive patients

Routine tests *All patients with hypertension*	**Additional tests** *All patients with hypertension if the test available*	**Extended tests** *Depending on specific indications*
Full blood count	Renal ultrasound with renal artery Doppler examination	Carotid artery ultrasound
Fasting plasma glucose level or OGTT if indicated	Urinary albumin-to-creatinine ratio (spot urine sample)	24-hour urinary sodium and potassium excretion
Serum total cholesterol, HDL cholesterol, LDL cholesterol, and triglyceride levels	Echocardiography	24-hour ECG monitoring if arrhythmia is present
Serum sodium, potassium, and uric acid level	Aldosterone-to-renin ratio after 2 hours in upright position	Ankle-brachial index measurement
Serum creatinine level (with GFR estimation)	Fundoscopy (patients with grade 2 and 3 hypertension)	Pulse wave velocity measurement
Urinalysis (with urine sediment examination)	Qualitative evaluation of proteinuria in women of childbearing age	Further search for cerebral, cardiac, renal and vascular damage
Serum ALT activity		
Serum TSH level		
12-lead ECG		

ALT — alanine aminotransferase; ECG — electrocardiogram; GFR — glomerular filtration rate; HDL — high-density lipoprotein; LDL — low-density lipoprotein; OGTT — oral glucose tolerance test; TSH — thyroid-stimulating hormone

Table VII. Risk factors disease used for stratification of the global cardiovascular risk

Non-modifiable	Modifiable
Male sex	Smoking — current or past
Age (men ≥ 55 years, women ≥ 65 years)	Hypercholesterolaemia
Premature menopause	Hyperuricaemia
Family history of premature CVD (men < 55 years, women > 65 years)	Overweight and obesity
	Sedentary lifestyle
Parental or family history of hypertension diagnosed at a young age	Psychosocial and socioeconomic factors
	Resting heart rate > 80 beats per minute

CVD — cardiovascular disease

Table VIII. Target organ damage, and metabolic, cardiovascular, and renal disease used for stratification of the global cardiovascular risk

Subclinical hypertension-mediated organ damage
Arterial stiffness: pulse pressure (in the elderly) ≥ 60 mm Hg PWV >10 m/s
Electrocardiographic evidence of LVH — Sokolov-Lyon index > 3.5 mV — R in aVL > 1.1 mV — Cornell voltage duration product >2440 mV × ms
Echocardiographic evidence LVH LVM index: > 50 g/m$^{2.7}$ in men, > 47 g/m$^{2.7}$ in women (height in metres raised to the power of 2.7) In subjects with normal body weight, LVM may be indexed for BSA: LVM/BSA > 115 g/m^2 in men, > 95 g/m^2 in women
Ankle-brachial index < 0.9
Chronic kidney disease — stage 3 with eGFR 30–59 mL/min/1.73 m^2 (BSA) or stage ≥ 4 with eGFR < 30 mL/min/1.73 m^2 (BSA)
Albuminuria 30–300 mg/24 h or urinary albumin–creatinine ratio 30–300 mg/g (3.4–34 mg/mmol) (preferably in morning spot urine)
Advanced retinopathy (haemorrhages or exudates, papilledema)
Diabetes
Uncomplicated diabetes (without organ damage)
Complicated diabetes (typical micro- and macroangiopathic complications)
Overt cardiovascular or renal disease
Cerebrovascular disease: ischemic stroke, cerebral haemorrhage, TIA
Cardiovascular disease: myocardial infarction, angina, myocardial revascularization
Presence of atherosclerotic plaques in imaging studies
Heart failure, including heart failure with preserved left ventricular ejection fraction
Symptomatic lower extremity peripheral arterial disease
Atrial fibrillation

BSA — body surface area; eGFR — estimated glomerular filtration rate; LVH — left ventricular hypertrophy; LVM — left ventricular mass; PWV — pulse wave velocity; TIA — transient ischemic attack

mary of all investigations performed in patients with hypertension is shown in Table VI.

3.3.4. Assessment of the global cardiovascular risk

In most patients, concomitant factors affecting the global cardiovascular risk may be detected at the time of the diagnosis of hypertension. The global cardiovascular risk should be evaluated in all patients with hypertension based on BP values (hypertension grade) and the presence of other classical and non-classical risk factors, subclinical target organ damage, cardiovascular disease, and chronic kidney disease (Tab. VII and VIII). The estimated risk is categorised as low, moderate, high, or very high. Interpretation of the level of risk (low, moderate, high, or very high) based on the Framingham model indicates that the

10-year absolute cardiovascular event risk is below 15%, 15–20%, 20–30%, and above 30%, respectively. Using the European Systematic Coronary Risk Evaluation (SCORE) model, the 10-year absolute cardiovascular death risk for the above risk categories is below 1%, 1–5%, 5–10%, and above 10%, respectively. Use of adjusted SCORE risk charts is recommended in the European populations. In Poland, it is the Pol-SCORE 2015 risk chart (Tab. IX). Use of the SCORE risk chart is recommended in subjects above 40 years of age free from cardiovascular disease and diabetes.

In all patients with hypertension, it is recommended to estimate the global cardiovascular risk, taking into consideration the stage of hypertensive disease. Stage 1 is an uncomplicated disease which may be accompanied by non-modifiable and modifiable risk factors for cardiovascular disease. Stage 2 is an asymptomatic disease with HMOD, such as chronic kidney disease (stage 3) or uncomplicated diabetes. Stage 3 is an overt hypertensive disease with complications, such as cardiovascular disease, more advanced chronic kidney disease (stage > 3), or complicated diabetes (Tab. X). In patients with masked hypertension, the global risk is similar to that in subjects with overt (office) hypertension. In contrast, the risk is lower in those with white-coat hypertension.

Global cardiovascular risk level affects the choice of the treatment strategy and intensity of hypertension treatment, and in particular the decisions regarding initiation of non-blood pressure-lowering therapy.

4. Therapeutic management

4.1. Overall goals and principles of the management

The basic goal of treatment in patients with hypertension is to reduce mortality and the global risk of cardiovascular and renal complications. In particular, drug treatment should reduce BP to values considered target levels in hypertensives or, if it is not feasible, as close to these values as possible. This is based on numerous observations that effective BP lowering reduces the relative risk of death (by 10–15%) and cardiovascular events (by 20%), particularly stroke (35%) and heart failure (40%), and delays progression of renal disease. These benefits are similar regardless of baseline severity of hypertension and cardiovascular risk, age, gender, and race. At the same time, global treatment strategy in the hypertensive patient should include correcting all other modifiable cardiovascular risk factors, in particular body weight, serum cholesterol level, serum uric acid level, and heart rate.

4.1.1. Indications for antihypertensive therapy

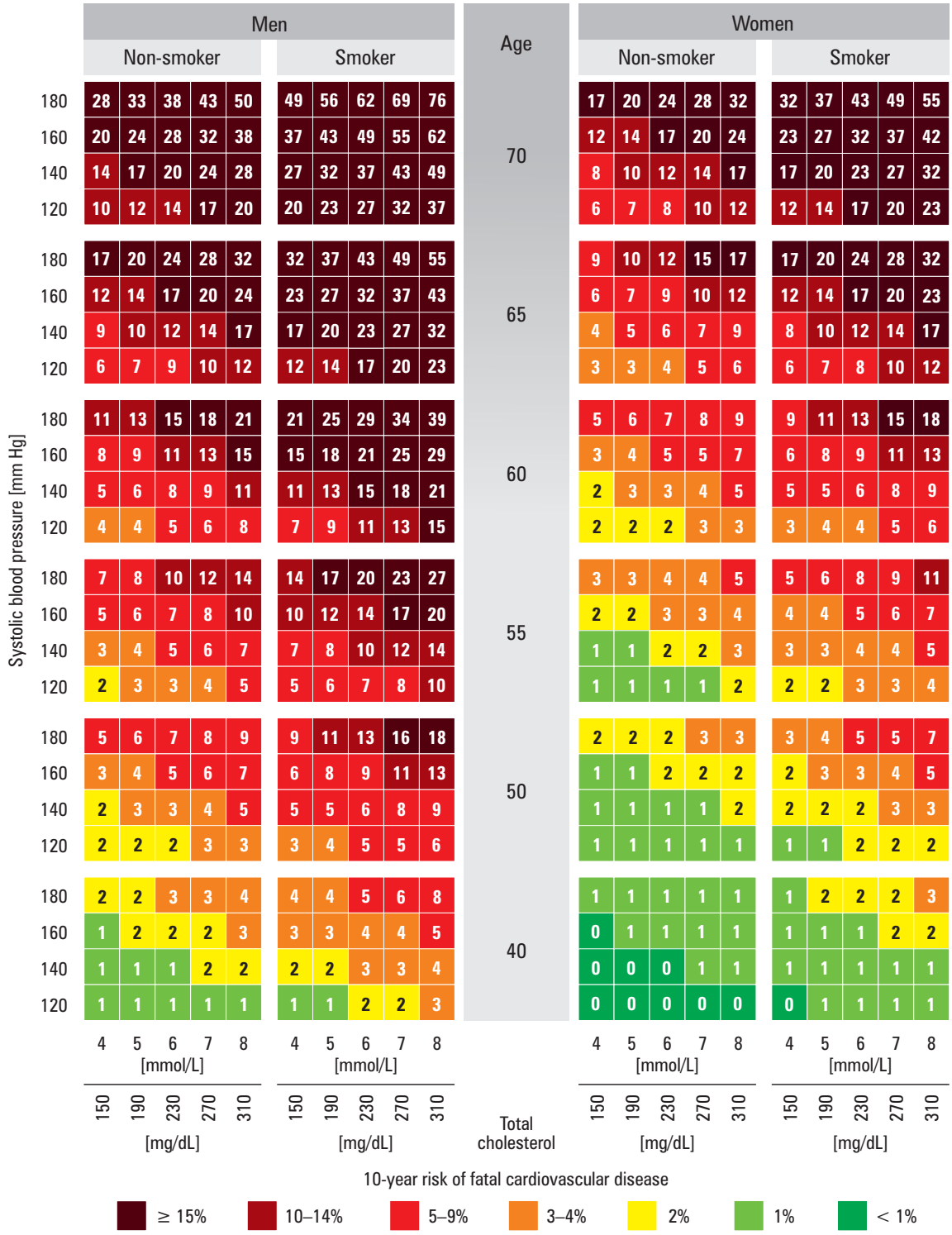
Blood pressure measurement is the most important component of the clinical evaluation before making a decision to initiate antihypertensive therapy. Clinical trials and metaanalyses indicate that the decision to initiate antihypertensive therapy should be based mostly on BP blood values and not evaluation of the global cardiovascular risk, as relative benefits are the same regardless of the baseline risk. Although absolute risk reduction is higher in patients with high baseline cardiovascular risk, their residual risk with adequate BP control is also the highest, and thus delaying or preventing progression to the highest risk group is an additional benefit of antihypertensive therapy in patients at lower baseline cardiovascular risk.

Non-drug treatment involving lifestyle changes is a necessary initial component of the management of hypertension and should be recommended at the first visit in all patients with suspected hypertension, including those with high normal BP. The decision to initiate drug treatment does not mean that lifestyle changes no longer need to be observed by the patient or pursued by the physician. At the same time, due to low patient compliance regarding lifestyle changes, institution of non-drug treatment should not delay the decision to initiate antihypertensive drug therapy, particularly in patients at higher cardiovascular risk.

If grade 3 (BP ≥ 180 and/or 110 mm Hg) or grade 2 (BP ≥ 160 and/or 100 mm Hg) hypertension is found, as confirmed by at least two measurements at one or two occasions, respectively, drug treatment should be initiated immediately along with non-pharmacological measures, prior to complete evaluation of the risk profile.

If the observed BP values are consistent with grade 1 hypertension (140–159/90–99 mm Hg), non-pharmacological measures should be instituted, and the decision to initiate drug therapy should be made after comprehensive risk stratification. In patients at high or very high cardiovascular risk, drug treatment should be initiated immediately. In patients at low to moderate cardiovascular risk, non-drug measures should be instituted for 3–6 months, followed by evaluation of the effects of non-drug treatment. If BP values remain at the grade 1 hypertension range, an additional verification of the diagnosis of hypertension by ABPM is indicated. In patients with HMOD and/or overt cardiovascular disease, it is not necessary to verify the diagnosis

Table IX. Assessment of the global cardiovascular risk using the Pol-SCORE risk estimation chart



Instructions on how to use the risk estimation chart

1. Find the appropriate table for given sex, smoking status and age, and then the cell nearest to the person's systolic blood pressure and total cholesterol level. The value given in the cell shows the risk in percent.
2. By moving upwards, you can estimate the effect of the exposure to risk factors during the lifetime.
3. Risk value ≥ 5% should be considered high.
4. By using this card, it is possible to show to the patient how his/her risk changes if he/she, e.g., stops smoking or reduces other risk factors.

Notes

1. Persons with established cardiovascular risk or diabetes ar at high risk regardless of the presence of other risk factors (i.e., there is no need to assess the risk using the SCORE risk estimation chart).
2. Risk may be higher than indicated by the chart in persons:

— close to the next age category;
— with asymptomatic atherosclerosis (e.g., detected by vascular ultrasound examination);
— with strong family history of premature cardiovascular disease;
— with low HDL cholesterol level, elevated triglyceride level, impaired glucose tolerance;
— obese and with a sedentary lifestyle.

Table X. Evaluation of the global cardiovascular risk in hypertensive patients based on the Framingham model

Hypertension stage	Blood pressure [mm Hg]			
	High normal BP (130–139/85–89)	Grade 1 hypertension (140–159/90–99)	Grade 2 hypertension (160–179/100–109)	Grade 3 hypertension (≥ 180/110)
Stage 1 No risk factors	Low	Low	Moderate	High
Stage 1 1–2 risk factors	Low	Moderate	Moderate/high	High
Stage 1 ≥ 3 risk factors	Low/moderate	Moderate/high	High	High
Stage 2 Target organ damage, diabetes without organ damage, CKD stage 3	Moderate/high	High	High	Very high
Stage 3 Overt cardiovascular disease, diabetes with organ damage, CKD stage ≥ 4	Very high	Very high	Very high	Very high

BP — blood pressure; CKD — chronic kidney disease

of hypertension by ABPM, as initiation of antihypertensive drug therapy is recommended both in grade 1 hypertension and in patients with white coat hypertension. In contrast, antihypertensive drug therapy is not recommended in patients with white coat hypertension if no HMOD is identified and/or cardiovascular risk is low to moderate. This recommendation is consistent with the 2018 ESC/ESH guidelines and reflects changes introduced in the latter compared to the 2013 version.

An opinion has been upheld that routine antihypertensive drug therapy is not necessary in patients with high normal BP (130–139/85–89 mm Hg). Only lifestyle changes are indicated in these subjects, and the use of antihypertensive medications in those at high or very high cardiovascular risk is justified by other reasons (treatment of cardiovascular disease, secondary prevention of cardiovascular events, or an attempt to induce regression of HMOD).

Based on an analysis of clinical trials and the most recent metaanalyses, the principles of initiating antihypertensive therapy in the elderly (> 65 years of age) are the same as in younger subjects. In particular, antihypertensive therapy in the elderly patients with grade 1 hypertension is considered necessary and not only reasonable. The HYVET study remains the only trial informing the management of the very elderly hypertensive patients (> 80 years of age). In this age group, antihypertensive therapy is recommended if SBP is ≥ 160 mm Hg.

The principles of initiating antihypertensive therapy are summarised in Tables XI and XII.

4.1.2. Target blood pressure

Target BP is a threshold value below which patient's BP should be kept during optimal antihypertensive therapy. Only once these target BP values are reached, there is no need for further treatment intensification. In the past, recommendations regarding target BP values were often changed with publication of the results of large trials comparing benefits of different target BP values during antihypertensive therapy. The currently prevailing opinion, reflected in the 2017 American Heart Association/American College of Cardiology (AHA/ACC) guidelines and the 2018 ESC/ESH guidelines, is that the optimal reduction of the global cardiovascular risk in younger patients (< 65 years of age) is obtained by reducing BP below 130/80 mm Hg in most patients with hypertension, including those with concomitant ischaemic heart disease, previous myocardial infarction, or stroke. This major change in the approach to setting target BP reflects the results of the large randomised SPRINT trial, in which the target SBP of < 120 mm Hg was associated with a cardiovascular morbidity and mortality risk reduction by about 30% compared to the conventional target SBP of < 140 mm Hg. As a result, some of the most recent metaanalyses that have included the SPRINT trial yielded similar conclusions. However, there is a significant concern over the validity of the SPRINT trial conclusions due to the automated office BP measurement technology used in the study, resulting in lower BP values due to elimination of the white coat effect, and the trial protocol that involved recruiting mostly patients

Table XI. Initiation of antihypertensive therapy in relation to blood pressure values and the global cardiovascular risk

<table>
<tr><th rowspan="3">Clinical profile</th><th colspan="4">Blood pressure [mm Hg]</th></tr>
<tr><th>High normal BP (130–139/85–89)</th><th>Grade 1 hypertension (140–159/90–99)</th><th>Grade 2 hypertension (160–179/100–109)</th><th>Grade 3 hypertension (≥ 180/110)</th></tr>
<tr><th colspan="4">Non-drug therapy and antihypertensive drug therapy</th></tr>
<tr><td>Stage 1
No risk factors</td><td>No intervention</td><td rowspan="3">Lifestyle changes, confirmation by ABPM*** if BP ≥ 140/90 after 3–6 months, then add drugs</td><td rowspan="3">Lifestyle changes + drug treatment starting from the 2nd visit (i.e., at the diagnosis)**</td><td rowspan="5">Lifestyle changes + drug treatment starting from the 1st visit**</td></tr>
<tr><td>Stage 1
1–2 risk factors</td><td>Lifestyle changes</td></tr>
<tr><td>Stage 1
≥ 3 risk factors</td><td>Lifestyle changes</td></tr>
<tr><td>Stage 2
Target organ damage, diabetes without organ damage, CKD stage 3</td><td>Lifestyle changes*</td><td rowspan="2">Lifestyle changes + drug treatment starting from the 1st visit**</td><td rowspan="2">Lifestyle changes + drug treatment starting from the 1st visit**</td></tr>
<tr><td>Stage 3
Overt cardiovascular disease, diabetes with organ damage, CKD stage ≥ 4</td><td>Lifestyle changes + consider drug treatment*</td></tr>
</table>

*In the high normal BP range, antihypertensive drugs are often indicated for reasons other than elevated BP (treatment of cardiac events, cardiovascular prevention, nephroprotection), without the need for reaching target BP < 130/80 mm Hg; **Reaching target BP values is indicated within 3 months; ***Or by home BP measurements; ABPM — ambulatory blood pressure monitoring; BP — blood pressure; CKD stage 3 — chronic kidney disease (eGFR 30–59 mL/min/1.73 m^2); CKD stage ≥ 4 — chronic kidney disease (eGFR < 30 mL/min/1.73 m^2); eGFR — estimated glomerular filtration rate

Table XII. Blood pressure (BP) thresholds for initiating antihypertensive therapy, target BP values, and undesirable levels of BP reduction in relation in relation to patient age and hypertension subtype

	Systolic-diastolic hypertension at < 65 years of age	Systolic-diastolic hypertension at 65–80 years of age	Systolic-diastolic hypertension at > 80 years of age	Isolated systolic hypertension
BP treatment threshold	≥ 140/90	≥ 140/90	≥ 160/90	≥ 140
Initial therapeutic target SBP	< 140	–	–	< 140*
Secondary therapeutic target SBP	< 130	< 140	< 150	< 130*
Undesirable SBP reduction	< 120	< 130	< 130	< 120*
Therapeutic target DBP	< 80	< 80	< 80	–
Undesirable DBP reduction	< 70	< 70	< 70	< 65

*In isolated systolic hypertension in the elderly and very elderly patients, thresholds for initiating antihypertensive therapy, target BP values, and undesirable levels of BP reduction apply for a given age. DBP — diastolic blood pressure; SBP — systolic blood pressure

who already received combined antihypertensive treatment and were well adapted to low BP values. These concerns were shared by the authors of the 2018 ESC/ESH guidelines who recommended **SBP below 140 mm Hg — i.e., the previous BP target — as the initial therapeutic target regardless of the cardiovascular risk level and the presence of complications. If BP reduction to these values is well tolerated, the secondary therapeutic SBP target has been set at below 130 mm Hg, but not lower than 120 mm Hg**, due to the J curve phenomenon observed in many clinical trials, i.e., relatively higher cardiovascular risk with too low achieved BP during antihypertensive therapy. It has also been noted that SBP values below 130 mm Hg should be achieved in most hypertensive patients.

At the same time, the target DBP level has been lowered to below 80 mm Hg, with on-treatment values in the 70–79 mm Hg range suggested for all hypertensive patients regardless of age and concomitant conditions. The 2018 ESC/ESH guidelines recommended these lower target BP levels also in patients with diabetes, previous stroke, or heart failure, although such patients were excluded from the SPRINT trial.

Despite the above concerns, these lower target BP levels were also adopted in the 2019 PTNT guidelines, as it can be argued that any divergent recommendations on this major issue between the Polish and European guidelines would be confusing for the practising physicians.

There are two exceptions from the target BP levels given above. **In the elderly patients (above 65 years of age), the recommended target BP values are below 140/80 mm Hg** (consistent with the 2018 ESC/ESH guidelines) **but not less than 130/70 mm Hg**.

In patients above 80 years of age, even more cautious SBP reduction to values below 150 mm Hg is recommended, based directly on the target SBP set in the HYVET trial which was the only successful study in this age group.

In patients with ISH, it is recommended to reduce SBP below 140 mm Hg, and if these BP values are well tolerated in patients below 65 years of age, to values below 130 mm Hg but not less than 120 mm Hg. Due to low DBP values and an advanced age of most patients with this subtype of hypertension, attempts to reduce SBP to the target values **should not lead to DBP reduction to values below 65 mm Hg**.

It is recommended to reduce BP below 140/90 mm Hg within 3 months, and then, if such a decision is made, to achieve rapidly the ultimate therapeutic target, i.e., BP values below 130/80 mm Hg. Rapid achievement of target BP values enhances patients' trust in their physician (with improved compliance) and increases cardiovascular risk reduction (VALUE study).

The criteria of antihypertensive therapy initiation, target BP values, and undesirable levels of BP reduction in relation to patient age and hypertension subtype are shown in Tables XI and XII.

4.1.3. Follow-up visits

Current practice indicates that in the initial treatment phase, while the diagnosis of hypertension is confirmed and treatment is initiated and intensified, follow-up visits should be set at monthly intervals, and after adequate BP control is obtained, their frequency may be reduced to once every 3 months. Intervals between follow-up visits should also depend on the degree of patient compliance, BP values, and the presence of target organ damage, concomitant disease, and other risk factors. The treatment regimen should be adjusted to patient lifestyle and needs, with simplification of the therapy, reduction of the daily number of tablets taken by the patient, involving family members in the therapeutic process, and tailoring treatment to the financial situation of the patient.

4.1.4. Specialist consultation

A specialist consultation should be considered if:

- target BP has not been reached during 6 months of therapy despite treatment with an optimal combination of 3 drugs in full doses (including a diuretic);
- previously well controlled BP worsened despite continued use of drugs and without an obvious cause indicated by the history;
- clinical findings are present that may indicate secondary hypertension.

4.1.5. Discontinuation of antihypertensive drug therapy

Discontinuation of antihypertensive drug therapy may be considered in the following situations:

- in patients with grade 1 hypertension and low cardiovascular risk who are fully compliant with non-drug therapy, following a long period (≥ 12 months) of good BP control as evidenced by both office and home measurements or ABPM;
- in young subjects in whom BP elevation was clearly associated with a stressful situation which is no longer present.

In these situations, drug doses or their number should be gradually and cautiously reduced but one should not withdrew all medications at once, and the patient requires frequent BP measurements.

4.2. Non-drug therapy

Non-drug therapy involves introduction of lifestyle changes that significantly reduce BP values in subjects with hypertension, increase effectiveness of drug therapy, and may reduce the risk of cardiovascular events and prevent development of hypertension in those with a family history of hypertension. However, due to poor patient compliance regarding lifestyle changes, their formal recommendation should never delay initiation of drug therapy in patients with target organ damage or very high cardiovascular risk.

Lifestyle changes that fulfil the above criteria **include weight reduction, appropriate diet with reduced fat intake (particularly of saturated fats)**

and increased vegetable and fruit intake, reduction of alcohol and salt intake, smoking cessation, and increasing regular physical activity.

4.2.1. Weight reduction and dietary recommendations

Excessive body weight (BMI > 25 kg/m^2 — overweight, and BMI > 30 kg/m^2 — obesity) is associated with an increased risk of hypertension, and weight reduction, and in particular reduction of abdominal obesity, not only results in BP lowering but also reduces dyslipidaemia and insulin resistance. A meta-analysis showed that a 5 kg body weight reduction was associated with BP reduction by 4.4/3.6 mm Hg, and the BP-lowering effect of weight reduction was more pronounced in obese subjects compared to those with near-normal body weight. Weight reduction may also have a beneficial effect on the effectiveness of antihypertensive therapy.

Reduction of excess body weight (optimal BMI slightly below 25 kg/m^2) should be obtained mostly by reduction of caloric intake and modification of diet composition (Tab. XIII). Patients are recommended to consume fruits and vegetables (300–400 g per day), fish (at least twice a week), low-fat dairy products, fibre, whole grain products and protein from plant sources, and to limit their saturated fat and cholesterol intake. These criteria are met by Mediterranean type diets.

Weight reduction efforts should also include regular exercise (Tab. XVII). In hypertensive patients, combining exercise with the Dietary Approaches to Stop Hypertension (DASH) study diet resulted in more pronounced body weight, BP and left ventricular mass reduction compared to the DASH diet only.

If reduction of excessive body weight proves difficult or body weight is regained following weight loss, multidisciplinary therapeutic approach including nutritional counselling is recommended.

Table XIII. Basic dietary recommendations for hypertensive patients, aiming for healthy body weight maintenance or reduction to normal values

Maintain daily caloric intake or reduce it in case of overweight or obesity
Increase intake of vegetables and other plant products (4–5 servings, 300–400 g/day) rich in potassium, e.g. tomatoes (300 g/day)*
Avoid products with high animal fat content (saturated fatty acids and cholesterol)
Substitute fish, fruits, vegetables, and other products containing unsaturated fatty acids for fatty animal products

*Excluding patients with renal failure or an increased risk of hyperkalaemia

Table XIV. Recommendations regarding salt intake in hypertensive patients

Reduce salt intake from usual 9–12 g to < 5 g per day (2 g Na)
To achieve this target: • discontinue using salt when preparing meals at home and at the table • consume meals prepared from fresh, natural products • avoid products containing sodium compounds used as preservatives

Available data, mostly from observational studies, do not indicate a higher risk of incident hypertension or higher BP values in persons who regularly consume coffee. In contrast, consumption of energy drinks, licorice-containing products, and foods with high fructose content (i.e., with added glucose-fructose syrup) should be avoided.

4.2.2. Salt intake

A causal relationship has been proven between salt intake and BP values. Excessive salt intake may contribute to resistance to antihypertensive treatment.

In patients with hypertension, reduction of salt intake by 4.4 g/day results in BP lowering by an average of 5.4/2.8 mm Hg. **Hypertensive patients should not consume more than 5 g of salt per day (≤ 2 g of sodium)** (Tab. XIV). BP-lowering effect of sodium intake reduction is seen in salt-sensitive subjects and is more pronounced in blacks, the elderly, and patients with diabetes, metabolic syndrome, and chronic kidney disease. Limiting salt intake also allows a reduction of the number and doses of antihypertensive drugs. Evaluation of sodium intake should be based on 24-hour urinary sodium excretion measurements, although this approach may be prone to a significant error. Despite an inverse relationship between sodium excretion and total mortality found in the general population, no data are available to indicate that reducing large or moderate salt intake in hypertensives might be harmful. In addition, salt intake reduction in the Trial of Hypertension Prevention (TOHP) study was associated with a lower risk of cardiovascular events.

4.2.3. Alcohol consumption

A linear relation is observed between alcohol intake and BP values and cardiovascular risk. Increased alcohol consumption predisposes to more frequent occurrence of strokes and attenuates the effect of antihypertensive drugs.

The recommendation to reduce alcohol intake (Tab. XV) should also include avoidance of binge drinking and introduction of alcohol-free days during the week.

Table XV. Recommendations regarding alcohol intake in hypertensive patients

Alcohol intake should be limited to: • in men: 20–30 g of pure ethanol daily but not more than 140 g per week (e.g., 2 glasses of wine 5 times per week) • in women: 10–20 g of pure ethanol daily but not more than 80 g per week (e.g., 1 glass of wine 5 times per week) **Note:** 10 g of pure ethanol corresponds to 250 mL of beer, 100 mL of wine, and 25 g of vodka
Avoid binge drinking
Set alcohol-free days during the week

Table XVI. Recommendations regarding smoking in hypertensive patients

Each patient should be asked about smoking at each visit
Active counselling should be undertaken regarding smoking cessation
Minimum anti-nicotine intervention should be performed at least once a year
If necessary, recommend: • nicotine replacement therapy • treatment with bupropione • treatment with cytisine • treatment with varenicline
If these measures fail, refer patients to addiction treatment centres
Weight gain should be prevented

4.2.4. Cigarette smoking

Smoking is one of the most important risk factors for cardiovascular disease and cancer. Smoking each cigarette induces a significant increase in BP and heart rate that persists for more than 15 minutes. Evidence is also available regarding harmful effects of passive smoking. In addition, smoking significantly increases the global risk of ischaemic heart disease, stroke and peripheral arterial disease, particularly in hypertensive patients in whom it attenuates the effect of antihypertensive drugs. Reducing smoking habit is an important component of cardiovascular risk reduction efforts in hypertensives (Tab. XVI). Smoking status of the patient should be ascertained at each visit. Smokers should be counselled to quit but the effectiveness of counselling is limited. For this reason, medications to help quit smoking should be considered in those who have difficulty with quitting. It remains controversial whether subjects unwilling to quit should be advised to use products that reduce exposure to the harmful components of tobacco smoke (tobacco heating systems instead of tobacco smoking), but these may be considered an intermediate step before quitting.

Table XVII. Basic recommendations regarding increased physical activity in hypertensive patients

Systematic exercise of moderate intensity for 30 minutes 5–7 days a week
Gradual increase in the duration of exercise up to at least 300 minutes per week
Endurance exercises (walking, running, swimming) supplemented with resistance exercises (e.g., squatting), adjusted to age, concomitant conditions, and patient preferences
Avoidance of strenuous isometric exercises (lifting heavy weights)
In patients with cardiac disease, exercise ECG testing and medically supervised rehabilitation may be necessary

ECG — electrocardiogram

4.2.5. Physical activity

Regular physical activity may reduce BP by 2–11 mm Hg depending on its type. In patients with hypertension, the most pronounced BP-lowering effect has been observed for endurance training. Regular physical activity, even of moderate intensity, also helps reduce overweight, increase general fitness, and reduce mortality and cardiovascular risk. Patients with hypertension should be advised to engage in at least 30 minutes of dynamic aerobic exercise of moderate intensity (e.g., jogging, brisk walking, cycling, swimming) on 5–7 days per week, with gradual increase of the exercise duration to 300 minutes per week. Resistance exercises (building up muscle strength with a small dynamic component) may supplement physical activity 2–3 times per week. Basic recommendations regarding increasing physical activity are summarised in Table XVII.

4.3. Antihypertensive medications

Large clinical trials have shown that effective BP control is the most important prerequisite for achieving the basic goal of treating hypertension, i.e., reduction of cardiovascular mortality and morbidity. In most hypertensive patients, drug treatment is necessary for that purpose along with lifestyle changes. The ESC/ESH guidelines, including the most recent 2018 document, have indicated for years that based on multiple metaanalyses, the benefits of major antihypertensive drug classes in terms of reducing mortality and the overall risk of cardiovascular events are similar, reflecting their similar antihypertensive efficacy. For this reason, a limited attention has been paid in the ESC/ESH guidelines to the issue of antihypertensive therapy individualisation, or specific indications for and contraindications to use of specific drug classes. In the opinion of the authors of the PTNT guidelines, an informed choice of specific drug classes may additionally optimise the treatment

of hypertension if one takes into account the effect of the drug(s) on other cardiovascular risk factors, existing subclinical target organ damage, cardiovascular disease, and other concomitant disease; patient age and gender; possibility of drug interactions and adverse effects; medication cost and financial situation of the patient; and previous physician experience with a given therapy (Tab. XXI). Thus, the position taken in the previous PTNT guidelines was upheld that the results of some large hypertension trials and their metaanalyses, along with pathophysiological clues and pharmacological differences, suggest a possibility of no class effect and/or better clinical utility of specific groups, subgroups, or individual drugs within drug classes, both major ones and others, in specific clinical situations, as indicated below when discussing specific drug classes and special patient populations, and in the table summary of antihypertensive drug therapy individualisation (Tab. XXII). These differences between guidelines in the approach to the choice of antihypertensive drugs have also affected the choice of single pill combinations recommended in the PTNT 2019 guidelines.

4.3.1. Major drug classes

A review of the scientific literature indicates that despite numerous attempts, no new antihypertensive drug classes that could both improve BP control and reduce cardiovascular risk have been introduced in the 21st century. The newest drug class — following renin inhibitors that have been introduced some years ago — is a combination of an angiotensin receptor blocker (ARB) and a neutral endopeptidase inhibitor (valsartan/sacubitril) but these drugs remain licensed only for use in heart failure. Although the benefits of antihypertensive drug therapy in reducing mortality and the risk of cardiovascular events are largely dependent on BP lowering per se, some antihypertensive drug classes are categorised as major, and other drug classes do not have this status. The criterion underlying this distinction is the presence or absence of data from large clinical trials showing significant benefits of a given class in reducing mortality and the risk of cardiovascular events in patients with hypertension. In the 2019 PTNT guidelines — in accordance with the 2018 ESC/ESH guidelines — it has been recommended that in uncomplicated hypertension, and in most cases of complicated hypertension and hypertension with concomitant diseases, except for hypertension in pregnancy, the first and second line choice for antihypertensive therapy should include medications from the five major drug classes with a proven beneficial effect on reducing cardiovascular mortality and/or the risk of cardiovascular events. These are thiazide/thiazide-like diuretics, β-blockers, calcium antagonists, angiotensin-converting enzyme inhibitors (ACEI), and ARB. In accordance with the above mentioned position regarding within-class differences between drugs, we continue to prefer certain subgroups within some major antihypertensive drug classes, with some modifications compared to the previous guideline edition (Tab. XVIII).

Table XVIII. Major classes of antihypertensive drugs

Five major classes of antihypertensive drugs
• with proven outcome benefits • recommended for combined treatment and available as SPC • used as monotherapy in specific situations
Thiazide diuretics (preferred thiazide-like agents)
β-blockers (preferred vasodilating and highly cardioselective agents)
Calcium antagonists (preferred dihydropyridines)
Angiotensin-converting enzyme inhibitors
Angiotensin receptor blockers

SPC — single pill combination

4.3.1.1. Thiazide/thiazide-like diuretics

Thiazide and thiazide-like diuretics are particularly useful in the elderly patients, subjects above 80 years of age (indapamide), those with ISH, and patients with a history of stroke. They are also often used as a part of combined antihypertensive treatment, particularly in patients with concomitant diabetes, those with renal dysfunction or with coexisting symptomatic heart failure. They are also a necessary component of three-drug combinations in patients who require such therapy.

A position has been upheld from the 2015 PTNT guidelines that the preferred drugs in this class should be thiazide-like diuretics (chlorthalidone, indapamide). Despite absence of head-to-head comparisons, which seem not to be feasible anymore, compared to conventional thiazide diuretics, more evidence of benefit regarding cardiovascular risk prevention in large-scale clinical trials (ALLHAT, ADVANCE, HYVET, PATS) has been obtained for thiazide-like diuretics in currently used lower doses that do not induce adverse metabolic effects, which has translated to an advantage of thiazide-like diuretics shown in some metaanalyses. In addition, thiazide-like diuretics exert a more potent and longer lasting BP-lowering effect, and their utility as monotherapy has been shown only for indapamide. An additional argument in favour of thiazide-like diuretics comes from the recent reports indicating somewhat

increased risk of skin cancers (except for melanoma) associated with long-term hydrochlorothiazide use, although it is not known whether this association also holds for other thiazide diuretics. The two thiazide-like diuretics mentioned above provide a choice based on the expected diuretic effect, ranging from moderate (indapamide) to large (chlorthalidone). Attention should be paid to possible metabolic (dyslipidaemia and the risk of new-onset diabetes) and electrolyte disturbances (hypokalaemia, hyperuricaemia, hyponatraemia, and hypercalcaemia), and respective laboratory parameters should be monitored during long-term therapy with conventional thiazide and thiazide-like diuretics due to the fact that an association was observed between long-term benefits of these drugs and the occurrence of the above mentioned disturbances during treatment. All single pill combinations of two- and three drugs including a thiazide-like diuretic that are available in Poland also include an ACEI (perindopril + indapamide ± amlodipine), which is important when choosing antihypertensive therapy in hypertensive patients with cardiac complications, and when the treatment needs to be intensified. It should also be noted that hydrochlorothiazide-containing single pill combinations are available in Poland, e.g., in a combination with a vasodilating β-blocker (nebivolol + hydrochlorothiazide), which, in light of some recent data, might lead to their recommendation, for example, in hypertensive women with concomitant osteoporosis.

4.3.1.2. Beta-blockers

Indications for the use of β-blockers in the treatment of hypertension include tachycardia or an elevated heart rate above 80 beats per minute (bpm), arrhythmia, evidence of a hyperkinetic circulation, particularly in younger subjects, and concomitant heart failure or coronary artery disease, particularly after a previous myocardial infarction, also in patients with concomitant chronic obstructive pulmonary disease (COPD).

In other clinical situations, β-blockers are not considered first-line drugs for the treatment of hypertension due to the fact that conventional cardioselective β-blockers (atenolol) were less effective in preventing cardiovascular events compared to the renin-angiotensin-aldosterone system (RAAS) inhibitors and calcium antagonists, particularly in regard to stroke prevention and inducing regression of left ventricular hypertrophy, which may be related to their weaker effect on central aortic pressure.

Due to introduction of elevated heart rate (> 80 bpm) as a cardiovascular risk factor and availability of bisoprolol in useful single pill combinations, the position from the previous PTNT guidelines has been modified and currently, two subgroups of $beta_1$-adrenergic blockers are preferred — vasodilating agents and conventional highly cardioselective β-blockers.

The preferred β-blocker in younger patients with uncomplicated hypertension (< 40 years of age), older hypertensive patients with concomitant ischaemic heart disease or heart failure, patients with hypertension and erectile dysfunction, and those with concomitant metabolic complications is a highly cardioselective $beta_1$-adrenergic blocker with vasodilating properties — nebivolol. It also seems justified to use this β-blocker for cardiovascular event prevention in patients with concomitant malignancy. This special position of nebivolol in the recent years has been reflected in the 2018 ESC/ESH guidelines which indicated a more favourable effect of nebivolol on central aortic pressure due to specific haemodynamic properties (smaller negative chronotropic effect and an additional vasodilating effect resulting from $beta_3$-adrenergic receptor activation). Of note, use of large nebivolol doses is now acceptable (up to 40 mg in the 2017 AHA/ACC 2017 guidelines), and 10 mg preparations have been introduced in Poland. The other vasodilating β-blocker, non-cardioselective carvedilol, is mostly useful in hypertension complicated with heart failure.

Conventional, highly cardioselective $beta_1$-adrenergic blockers, particularly bisoprolol, are preferentially used in hypertensive patients with an elevated heart rate (> 80 bpm), concomitant ischaemic heart disease and/or heart failure, arrhythmia, and in case of combined antihypertensive therapy using single pill combinations. In these cases, due to the need to achieve desired heart rate reduction, conventional, highly cardioselective β-blockers, including bisoprolol, betaxolol, and long-acting metoprolol preparations, may be more useful than vasodilating $beta_1$-adrenergic blockers.

4.3.1.3. Calcium antagonists

Most large-scale clinical trials (ALLHAT, ASCOT, VALUE, ACCOMPLISH) that documented a beneficial effect of calcium antagonists on the cardiovascular risk reduction used dihydropyridines and this subgroup is much more commonly used in the clinical practice. For these reasons, the position has been upheld from the 2015 PTNT guidelines that dihydropyridines should be preferred for antihypertensive therapy. A negative inotropic effect of non-dihydropyridine calcium antagonists may be harmful in patients with heart failure or reduced left ventricular ejection fraction. In particular, the ef-

ficacy and safety of long-acting dihydropyridines in the elderly, including patients with ISH (Syst-Eur), patients with peripheral arterial disease, and hypertensive patients with concomitant COPD or asthma should be noted. An important advantage of calcium antagonists is their neutral metabolic effect, and thus these drugs are useful in combination with RAAS inhibitors in patients with concomitant lipid and/or carbohydrate metabolism disturbances. Some metaanalyses suggest high efficacy of calcium antagonists in the prevention of atherosclerosis, and clinically in the prevention of stroke, but this was not confirmed in the studies on secondary stroke prevention. On the other hand, metaanalyses also indicate that these drugs are less effective in preventing heart failure and reducing proteinuria. Although most evidence for cardiovascular risk reduction in large-scale clinical trials was obtained for amlodipine, use of this drug is associated with a relatively high rate of leg oedema and thus lercanidipine and lacidipine are alternative long-acting but better tolerated drugs of this class. New reports highlight additional pleiotropic effects of new dihydropyridines, such as a nephroprotective effect of lercanidipine, which is not typical for other dihydropyridine calcium antagonist, or event their additional effect on the T-type calcium channels. At the same time, some studies reported potentially better prevention of dementia by older drugs of this class (amlodipine). Both amlodipine and lercanidipine are available in single pill combinations with RAAS inhibitors.

4.3.1.4. Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers

An ACEI or ARB is a necessary component of first-line antihypertensive therapy in the basic treatment algorithm. Both these classes of the renin-angiotensin system (RAS) inhibitors also have most indications in special patient populations.

Metaanalyses suggest additional benefits of ACEI in the prevention of cardiac events beyond their BP lowering effect that may be associated with bradykinin-mediated effects of these drugs.

Differences between ACEI and ARB in regard to cardiovascular event prevention have not been commented in the 2018 ESC/ESH guidelines, although since publication of the previous edition of these guidelines, three important metaanalyses were published, focusing on different patient populations, i.e., hypertensives, patients with hypertension and/or ischemic heart disease, and diabetic patients, which all showed an advantage of ACEI over ARB. The first of these metaanalyses suggested a special position of perindopril among ACEI, particularly in the context of combined treatment and use of single pill combinations as recommended in the 2018 ESC/ESH guidelines. Taking into account consistent results of these metaanalyses, the present 2019 PTNT guidelines upheld a modified position from the previous edition, indicating that ACEI should be preferred over ARB (with indications retained for telmisartan) in patients with hypertension and high cardiovascular risk, particularly due to concomitant cardiac complications. This position has been reflected in the table that summarises individualisation of antihypertensive drug therapy, as according to the cardiac societies' guidelines, ACEI are preferred in patients with ischaemic heart disease and/or heart failure with elevated BP values. In contrast, ACEI and ARB are considered to have equivalent positions in hypertension without cardiac complications, which is also consistent with the European guidelines.

The above position was considered valid despite a metaanalysis published last year which suggested an equivalent cardiovascular risk reduction by ACEI and ARB with better tolerance of the latter. These results may be explained by the fact that this metaanalysis only included head-to-head studies, while excluding placebo controlled trials and combined treatment studies, and thus, it was mostly based on the only large ONTARGET study which directly compared the effect of ramipril and telmisartan on cardiovascular mortality and morbidity in high cardiovascular risk patients and showed no difference between these two drugs.

Of note, in the SMILE-4 study, a sulfhydryl (-SH) group-containing ACEI zofenopril was more effective compared to ramipril, the comparator in the ONTARGET study, Further analyses from the SMILE studies also showed the efficacy of zofenopril in comparison with some other ACEI in patients with post-infarction left ventricular dysfunction, particularly those with hypertension.

Angiotensin-converting enzyme inhibitors also have a strong position in combination with a thiazide-like diuretic [as a single pill combination (SPC) of perindopril + indapamide], which stems from the results of clinical trials in patients with hypertension and diabetes (ADVANCE) and in patients with a history of stroke (PROGRESS). In addition, only these RAS inhibitors (perindopril) are available in single pill combinations containing the preferred subgroup of thiazide-like diuretics.

Angiotensin receptor blockers are in turn preferred in patients with hypertension and target organ damage, concomitant renal disease (including diabetic nephropathy), and in those with a history of stroke, with some metaanalyses suggesting that ARB prevent

Table XIX. Other drug classes useful as third- to fifth-line drugs in the treatment of hypertension and in special situations

Loop diuretics
Aldosterone antagonists
α-blockers
Central sympatholytic agents
Imidazoline receptor antagonists
Peripheral sympatholytic agents

stroke better than myocardial infarction. ARB are also the antihypertensive drug class which induces least common adverse effects and as a result, they are least commonly discontinued by the patients. For this reason, they are recommended in patients with cardiac complications as an alternative to ACEI if the latter are not tolerated.

4.3.2. Other antihypertensive drugs

Due to lack of prospective studies evaluating the effect on mortality and cardiovascular risk during antihypertensive therapy, other drug classes, such as α-blockers, aldosterone antagonists, loop diuretics, imidazoline receptor agonists, and peripheral and central sympatholytic drugs, are currently not recommended as first- and second-line antihypertensive medications. However, this does not preclude use of these drugs during combination therapy if indicated individually, and in resistant hypertension, usually as third- to fifth-line drugs (Tab. XIX). Similarly to major antihypertensive drug classes, differences exist in regard to efficacy, safety, pharmacokinetic differences, and adverse effects also between specific drugs within other groups of antihypertensive medications in specific clinical situations. This is particularly the case for torasemide among loop diuretics (more favourable pharmacokinetics, potential additional pleiotropic effects), methyldopa among sympatholytic drugs (safety in the treatment of hypertension in pregnancy), and spironolactone (higher efficacy) and eplerenone (less adverse effects) among aldosterone antagonists. It should be noted, however, that eplerenone is not licensed to treat uncomplicated hypertension in Poland. In patients with concomitant benign prostatic hyperplasia, uroselective tamsulosin should be rather used if hypertension requires one- or two-drug therapy, while resistant hypertension may sometimes require doxazosin use as this α-blocker exerts a BP-lowering effect.

4.4. Drug treatment algorithm

Previous antihypertensive drug algorithms recommended in the European and American guidelines, and thus also in the PTNT guidelines allowed antihypertensive drug therapy to be initiated using one (monotherapy) or two drugs (combined therapy using two medications or a single pill combination) chosen from major drug classes, followed by further modifications including medication substitution and increases in the number or dose of medications. The decision to initiate treatment with monotherapy or combined therapy depended on the severity of hypertension and the degree of BP lowering necessary to reach target BP (PTNT guidelines) and/or cardiovascular risk (ESC/ESH guidelines). In practice, as indicated by the epidemiological studies, such an approach allowed good BP control in about 25% of hypertensive patients in Poland, and in about 40% of patients who declared willingness to be treated. Thus, there was a need for a modified approach to antihypertensive drug therapy, as indicated in the 2017 PTNT expert consensus document. In the 2018 ESC/ESH guidelines, a completely new algorithm for the management of hypertension has been adopted, recommending two-drug SPC as the initial treatment in a large majority of patients, followed by treatment intensification by using three-drug SPC if required. Initiating treatment with monotherapy has been reserved for rare, clearly defined situations. This management algorithm (Fig. 1) reflects major changes in the antihypertensive drug treatment strategy: wide use of combined treatment using SPC as the initial treatment, despite lack of appropriate licensing of most SPC preparations, and simplified treatment intensification with rapid transition to three drug therapy using SPC. It also indicated that such treatment strategy, with the addition of spironolactone if required, may allow adequate BP control in most patients. Practical management algorithms based on this strategy, with some modifications regarding treatment intensification and wider indications for monotherapy in the elderly patients, taking into account differences between various age groups, are shown in Figures 2, 6 and 7 in the present document.

4.4.1. Combined antihypertensive therapy using single pill combinations

Large-scale clinical trials indicate that in about 60% of hypertensive patients, good BP control may be achieved by using two antihypertensive medications with dose escalation if required, and in further 20% of patients, target BP values may be achieved by using three antihypertensive medications, provided that adequate compliance is achieved and maintained long-term. For these reasons, according to the new management algorithm, **antihypertensive therapy**

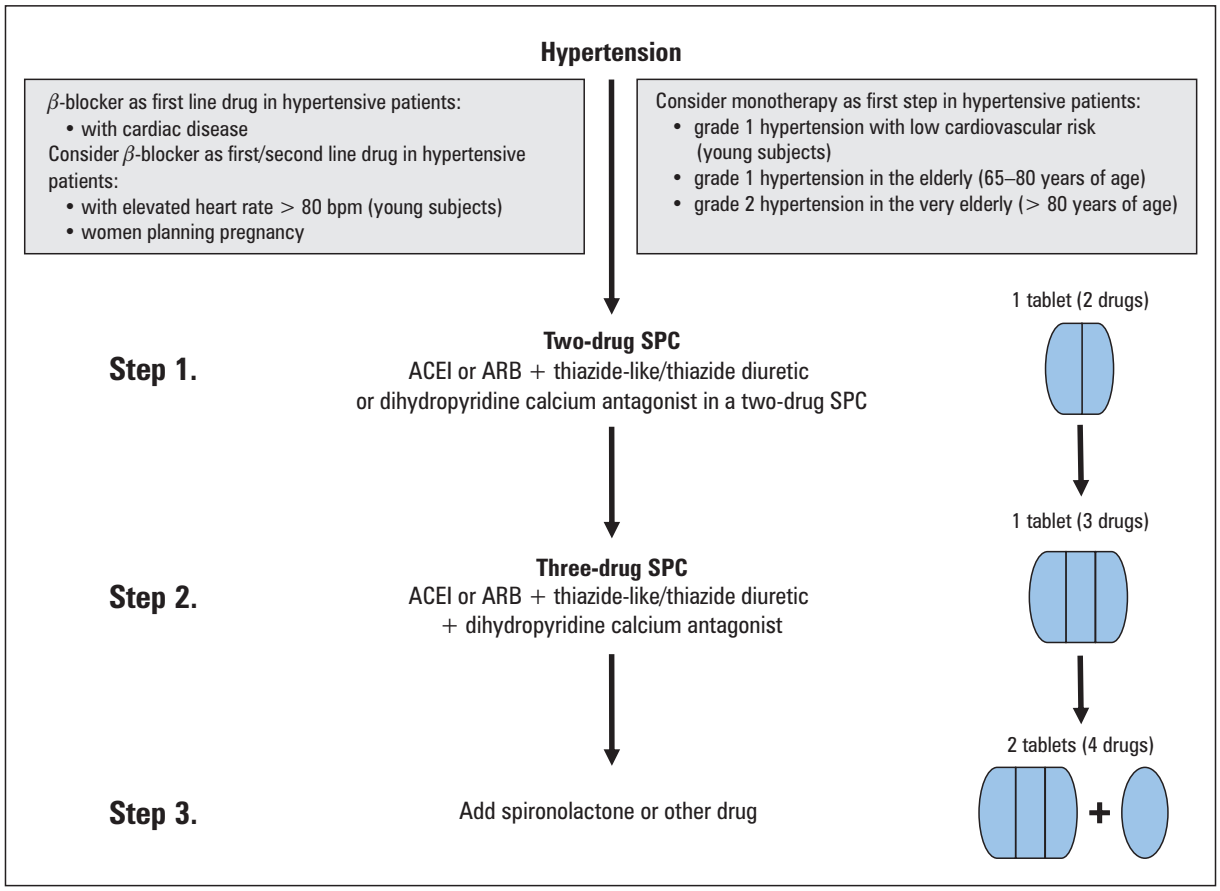


Figure 1. Basic management algorithm for antihypertensive drug therapy in patients with uncomplicated hypertension, hypertension with target organ damage, after a stroke, and with concomitant diabetes or peripheral arterial disease according to the 2018 ESC/ESH guidelines. ACEI — angiotensin-converting enzyme inhibitor; ARB — angiotensin receptor blocker; bpm — beats per minute; SPC — single pill combination

in most patients below 65 years of age is initiated (Step 1) with combined treatment using one of first-line SPC, i.e., combinations of an ACEI or ARB with a dihydropyridine calcium antagonist or a thiazide-like/thiazide diuretic in standard doses. If the initial therapeutic target is not reached, possible options (Step 2) include increasing drug doses of the initially selected SPC, with escalation to maximal doses, or switching to a three-drug SPC in standard doses. Further treatment intensification (Step 3) involves increasing drug doses of the selected three-drug SPC to maximal doses (Fig. 2). The rate of these treatment modifications and the approach to dose escalation depend on baseline BP values and the observed BP lowering, with the aim of achieving the initial therapeutic target (BP < 140/90 mm Hg) within 3 months. Further rapid treatment intensification is recommended over the next months if BP reduction below 130/80 mm has not been achieved. If SBP falls below 120 mm Hg, it is possible to reduce the dose of one of the SPC components.

Due to much increased importance of SPC in the 2017 AHA/ACC guidelines, the 2018 ESC/ESH guidelines, and the present 2019 PTNT guidelines, the role of various groups and specific drugs largely depends on the availability of SPC containing these drugs.

Major two-drug combinations used for treatment initiation in patients with uncomplicated hypertension, and hypertensive patients with target organ damage, metabolic disturbances or a previous stroke include:

— ACEI + dihydropyridine calcium antagonist;
— ACEI + thiazide/thiazide-like diuretic;
— ARB + thiazide diuretic;
— ARB + calcium antagonist.

These combinations are well tolerated, effective in terms of BP lowering and cardiovascular risk reduction, and available in Poland as SPC with a large range of available doses.

Both thiazide/thiazide-like diuretic and dihydropyridine calcium antagonist increase activity of the RAS, which potentiates the BP-lowering effect of

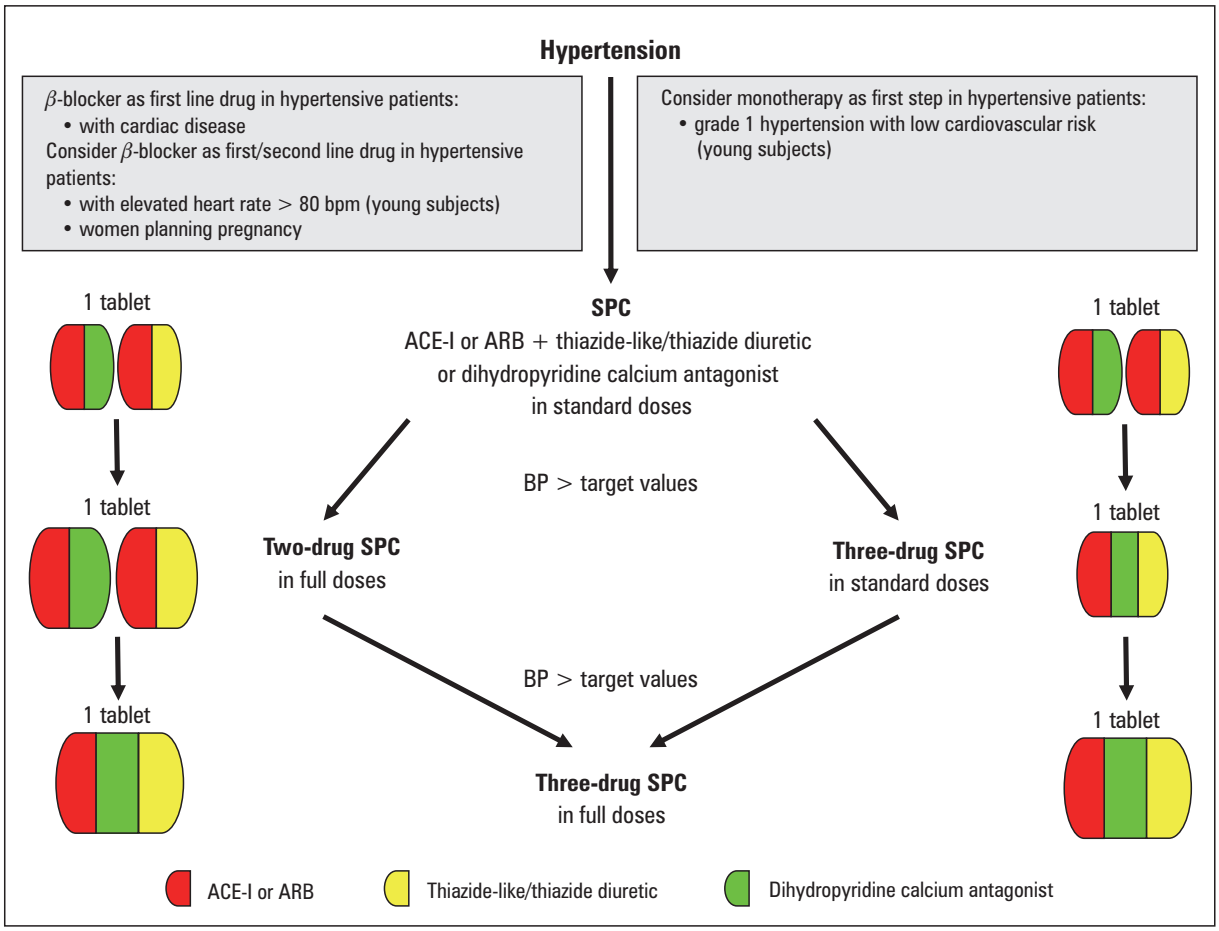


Figure 2. Algorithm for antihypertensive drug therapy in patients with hypertension below 65 years of age. ACEI — angiotensin-converting enzyme inhibitor; ARB — angiotensin receptor blocker; BP — blood pressure; bpm — beats per minute; SPC — single pill combination

a RAS inhibitor. In addition, rates of typical adverse effects of diuretics (hypokalaemia, metabolic effects) and dihydropyridine calcium antagonists (peripheral oedema) decrease with concomitant use of a RAS inhibitor.

In a direct comparison, better cardiovascular risk reduction was shown for a combination of ACEI + calcium antagonist compared to a combination of ACEI + thiazide diuretic (ACCOMPLISH). No SPC containing ARB + thiazide-like diuretic are available, and the only SPC containing ACEI + thiazide-like diuretic is a combination of perindopril and indapamide.

In turn, multiple available SPC of an ARB and a diuretic contain only hydrochlorothiazide. The BP-lowering efficacy and clinical utility of these combinations was shown in multiple trials (LIFE, VALUE).

Major three-drug combinations used in the new algorithm for the management of hypertension and available as three-drug SPC in Poland are:

— **ACEI + thiazide-like diuretic + calcium antagonist;**
— **ARB + thiazide diuretic + calcium antagonist.**

Each of these combinations is currently available in Poland as only one SPC, i.e., perindopril + indapamide + amlodipine and valsartan + hydrochlorothiazide + amlodipine. Studies showed improved BP control when using these combinations compared to two-drug combinations. Randomised trial analyses also indicate cardiovascular risk reduction with the former combination.

Two-drug combinations used in special patient populations or for multidrug therapy and available as SPC in Poland include:

— **dihydropyridine calcium antagonist + β-blocker;**
— **thiazide-like diuretic + calcium antagonist;**
— **β-blocker + ACEI;**
— **thiazide diuretic + vasodilating β-blocker.**

A combination of β-blocker and dihydropyridine calcium antagonist is used in young subjects, particularly women of reproductive age, in whom RAAS inhibitors should be avoided. A combination of calcium antagonist and thiazide-like diuretic is used in the elderly patients and those with ISH, and a combination of β-blocker and ACEI is recom-

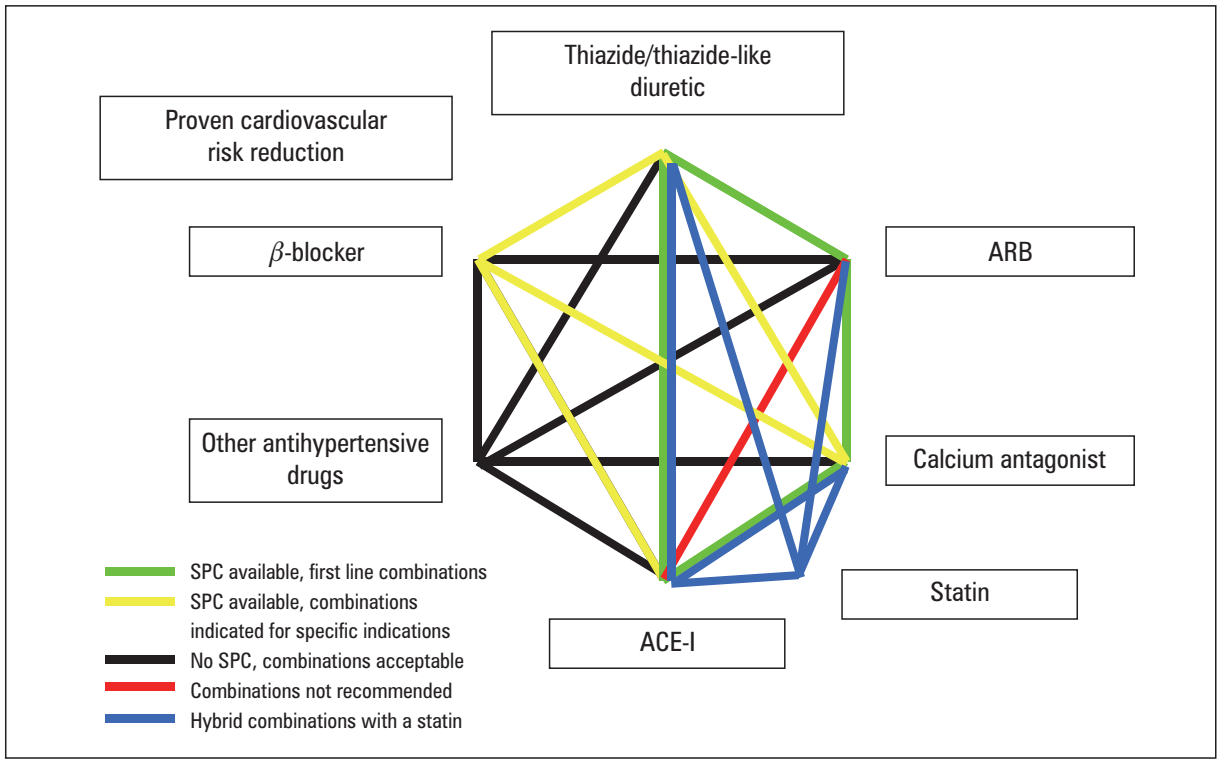


Figure 3. Two-drug combinations of antihypertensive drugs, taking into account their utility and availability of single pill combinations (SPC). ARB — angiotensin-receptor blocker; ACEI — angiotensin-converting enzyme inhibitor

mended for antihypertensive therapy in patients with hypertension and cardiac complications (ischaemic heart disease, heart failure). In the present guidelines, similarly to the 2018 ESC/ESH guidelines, a combination of vasodilating β-blocker and thiazide diuretic has been considered useful due to the results of many clinical trials that documented its benefits versus placebo in the early era of evidence-based medicine. However, this combination is mostly used in hypertension with heart failure. It should be remembered that this combination offers less effective cardiovascular event prevention (ASCOT and LIFE studies) and may be associated with a higher risk of metabolic disturbances and new-onset diabetes, although this risk is mitigated if a vasodilating β-blocker is used.

Finally, the armamentarium of combined antihypertensive therapy also includes SPC in substandard doses (lower than those used for monotherapy), used for initiating treatment in patients who require greater caution, such as the elderly. Currently, such combinations of an ACEI (perindopril) with a thiazide-like diuretic or a dihydropyridine calcium antagonist are available in Poland.

Note: RAAS inhibitors should be very cautiously combined with potassium-sparing diuretics as this combination may lead to hyperkalaemia. The two-drug combination of **ACEI + ARB is not recommended** due to an increased risk of adverse renal effects without additional benefits (ONTARGET) or even with an increased risk (ALTITUDE). Non-dihydropyridine calcium antagonists (verapamil and diltiazem) combined with β-blockers predispose to bradycardia and heart failure, and diuretics combined with α-blockers predispose to orthostatic hypotension. Possible two-drug combinations for the treatment of hypertension are summarised in Figure 3, taking into account their utility and availability of SPC, including so-called hybrid SPC (antihypertensive medication + statin).

Such a radical expansion of indications for combined antihypertensive treatment and a strong position of SPC stem from multiple benefits of such therapy, summarised in Table XX. Some of the benefits of SPC (lower doses of individual drugs, which translates to better tolerance, and more rapid achievement of BP control) are in fact advantages of combined treatment. It should be noted that the metaanalysis by Wald et al. showed that the additional BP-lowering effect of combining drugs from two different classes in nearly 5-fold higher compared to doubling the dose of a single drug. This is also important in the context of VALUE study results which showed a significantly higher cardiovascular risk reduction in those patients in whom BP was controlled within the

Table XX. Advantages of combined antihypertensive drug therapy and single pill combinations

More potent BP reduction
More rapid and more frequent attainment of BP control
Lower doses of individual drugs
Better tolerance (fewer adverse effects)
Fewer tablets
More convenient therapy
Lower costs
Improved compliance
Reduced therapeutic inertia

BP — blood pressure

initial 6 months of treatment. Further benefits are directly related to the SPC form, i.e., lower number of tablets and convenient dosing, and translate to the most important advantage of SPC, i.e., improved patient adherence to treatment, including both compliance and persistence, which leads to a further increase in the antihypertensive treatment efficacy (STITCH and ACCOMPLISH studies).

At the same time, previously postulated lower flexibility of SPC dosing used to be related to the fact that many such preparations were available in only one combination of doses, as also reflected by the former term "fixed dose combination" (FDC), implying precisely defined, fixed proportions of the components of a combined preparation. This is, however, no longer true with the current availability of different dose combinations of a given SPC. Currently, most SPC have from 3 (two-drug SPC) to 6 (three-drug SPC) dose combinations available, which allows flexible treatment modification, particularly with the present recommendation of dose escalation every 2–4 weeks if BP remains inadequately controlled in the initial treatment phase to reach target BP.

4.4.2. Indications for monotherapy

Indications for initiating therapy with a single drug have been much restricted as in monotherapy, most current antihypertensive agents lower BP by less than 20/10 mm Hg and such a BP-lowering effect is seen in only about 50–60% of patients. For these reasons, **monotherapy may only be considered in specific situations**. The first of these is **grade 1 hypertension in subjects at low cardiovascular risk**. In practice, these are young subjects with SBP of 140–150 mm Hg, often with elevated heart rate, who require either a vasodilating β-blocker (more beneficial effect on central aortic pressure) or, if normalisation of heart rate proves difficult, a conventional cardioselective β-blocker (stronger negative chronotropic effect). Another such situation is **grade 1 hypertension in the elderly subjects, or grade 2 hypertension in subjects above 80 years of age**, due to higher target BP values and potential consequences of hypotension. In those patients, dihydropyridine calcium antagonists or thiazide-like diuretics may be considered, with preference of indapamide in those above 80 years of age. The pathophysiological basis for such initial drug choice is the fact that RAAS inhibitors and β-blockers are more frequently effective in younger patients, often with so called resistance, high-renin, or hyperkinetic hypertension, while thiazide-like diuretics and calcium antagonists are more effective in older patients who are more frequently characterised by volume or low-renin hypertension. Patient gender may also be factor, as RAAS inhibitors should be avoided in women of reproductive age, and β-blockers or calcium antagonists should be preferred instead.

It should be remembered that treatment benefits are mostly related to BP lowering, and thus medications characterised by a high trough-to-peak (T/P) ratio are preferred, particularly in monotherapy, as they provide better 24-hour BP control and may be given once daily.

Increasing the drug dose to the maximum dose exerts little additional BP lowering effect but largely increases the risk of adverse effects. Thus, if monotherapy using a standard drug dose is not effective enough, adding a second drug by switching to an appropriate SPC has been considered the optimal next step among possible options.

4.4.3. Masked hypertension and chronotherapy of hypertension

Studies based on ABPM indicate that in many patients, additional cardiovascular risk is associated with masked hypertension. This mostly involves elevated BP values during the night and may be associated with a non-dipping BP pattern. The 2018 ESC/ESH guidelines were the first to indicate that antihypertensive therapy should be used in patients with masked hypertension, while the PTNT guidelines have recommended chronotherapy in this patient group for many years. Typical morning dosing of long-acting antihypertensive drugs may not allow adequate BP control during the night and may not correct these disturbances of the circadian BP profile. In these circumstances, i.e., with the non-dipping BP pattern and masked nocturnal hypertension, modification of the timing of antihypertensive drug administration with evening drug dosing should be considered (Fig. 4). As this approach to chronotherapy of hypertension, first suggested in the 2011 PTNT

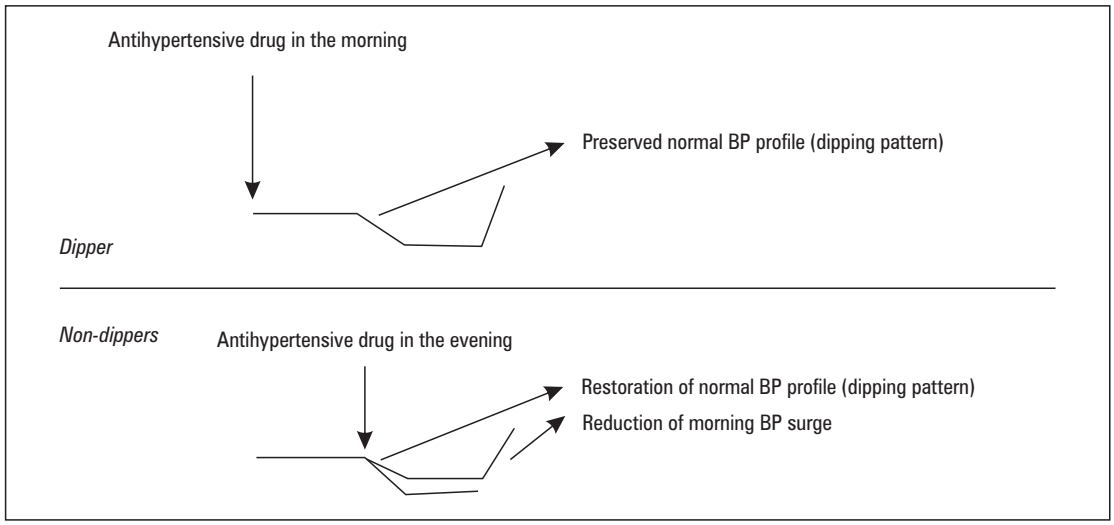


Figure 4. Suggested timing of antihypertensive drug administration in relation to the 24-hour blood pressure (BP) profile

guidelines, has become popular, it should be stressed that such evening dosing of antihypertensive drugs must be based on an evaluation by ABPM (non-dipping pattern) and should mostly involve dosing of RAS inhibitors. Evening dosing of ARB or ACEI (with a general preference of shorter-acting drugs and those tested in chronotherapy studies, e.g., ramipril and valsartan) was associated with an improved circadian BP pattern and reduced microalbuminuria. It also proved safe in large-scale clinical trials (HOPE, Syst-Eur). Evening dosing of antihypertensive drugs is contraindicated in patients with glaucoma. In view of a strong tendency to prefer SPC, it should be stressed that the above mentioned RAS inhibitors are components of various SPC, and combinations with a dihydropyridine calcium antagonist may be administered at the evening, as amlodipine provides a uniform BP-lowering effect over 24 hours regardless of the timing of its administration.

Table XXI. Individualization of drug therapy

When choosing (or avoiding) any particular drug combination (or drug), the following should be taken into consideration:
• availability of single pill combinations (SPC)
• possibility of initiating and intensifying therapy using SPC
• presence of cardiovascular and renal disease
• presence of other concomitant conditions
• presence of other cardiovascular risk factors and target organ damage
• demographic factors (age, gender, race, body weight)
• 24-hour blood pressure-lowering efficacy of a drug
• drug adverse effect profile
• drug cost — but never at the price of lower treatment effectiveness and tolerance
• previous physician and patient experience with a given drug (drugs)

5. Special patient populations

5.1. Individualisation of antihypertensive therapy

The approach to drug therapy adopted in the current and previous guidelines gives much emphasis to its individualisation (Tab. XXI).

The choice of first-line therapy is important due to potential benefits beyond BP lowering documented in large-scale clinical trials in specific clinical situations. At the same time, current recommendations regarding individualisation of antihypertensive therapy must be consistent with the new management algorithm and include use of different SPC. With so many different available SPC, this is possible for the most common cardiovascular and renal complications and metabolic disturbances accompanying hypertension (Fig. 5). Individualisation of antihypertensive therapy may also offer additional benefits, or allow avoiding adverse effects in specific conditions due to different pharmacological properties of antihypertensive medications. Specific indications for and contraindications to different drug classes are shown in Tables XXII and XXIII.

5.2. Hypertension in the elderly

Large clinical trials and metaanalyses indicate that antihypertensive therapy in patients above 65 years of age significantly reduces the stroke rate, heart failure incidence, and cardiovascular mortality. Although patients with baseline SBP ≥ 160 mm Hg were recruited to the available clinical trials specifically targeting this age group, and SBP was lowered in these

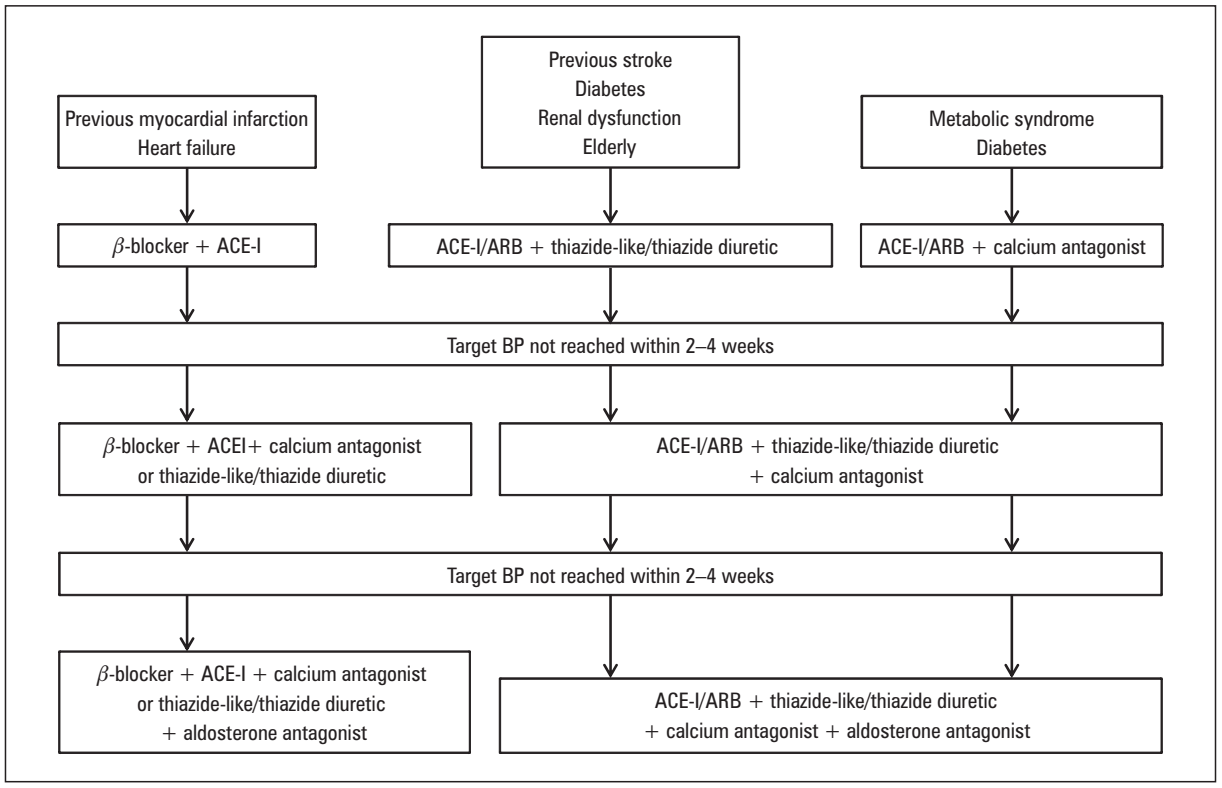


Figure 5. Preferred choices of single pill combinations/combined therapy and intensification of antihypertensive drug therapy in relation to concomitant conditions. ACEI — angiotensin-converting enzyme inhibitor; ARB — angiotensin-receptor blocker; BP — blood pressure

studies below 150 mm Hg but not below 140 mm Hg, the elderly subjects also comprised a majority in multiple clinical trials that confirmed benefits of antihypertensive therapy with BP lowering below 140/90 mm Hg, regardless of baseline severity of hypertension. Despite the fact that the elderly patients comprised a large group of the SPRINT trial participants, concerns over this study led to a recommendation of target BP below 140/80 mm Hg, if the patient is in a good overall condition and tolerates the therapy well, in both the 2018 ESC/ESG guidelines and now the 2019 PTNT guidelines. It is not recommended to lower SBP below 130 mm Hg.

Benefits of antihypertensive therapy in the elderly are similar to those obtained in younger age groups. However, due to a reduced adaptive capacity of the cardiovascular system and the risk of orthostatic hypotension, therapy should be more cautious, and target BP values should be reached more gradually. Due to the risk of orthostatic hypotension and falls, BP in the elderly hypertensive should be measured after 1 and 3 minutes of standing (orthostatic testing) in the following situations:

- therapy initiation;
- treatment change;
- history of falls;
- dizziness or near-fainting;
- concomitant diabetes.

It should also be noted that the HYVET study remains the only dedicated study (and not a subanalysis) that showed benefits of antihypertensive therapy in patients above 80 years of age. For this reason, a recommendation has been upheld that in this patient group, antihypertensive therapy should be initiated if SBP is 160 mm Hg or above, aiming for target SBP below 150 mm Hg (Tab. II). However, due to differences in the general health condition of these individuals, the decision to initiate therapy should be individualised, and BP lowering should be gradual and carefully monitored by the physician. A decision to initiate antihypertensive therapy in patients with frailty syndrome, which is common among those above 80 years of age,

The basic principles of non-drug therapy in the elderly hypertensives are the same as in younger subjects but limitations due to impaired mobility and reduced fitness, precluding regular exercise, should be borne in mind.

All major classes of antihypertensive medications were tested in large-scale clinical trials in the elderly patients, and recent metaanalyses do not indicate any differences in the efficacy of antihypertensive

Table XXII. Preferred first (I) and second (II) choice antihypertensive drug classes* in specific conditions

Clinical condition	Preferred first and second choice drugs								
	TD	BB	CA-dhp	CA-ndhp	ACEI	ARB	AA	LD	MD
Left ventricular hypertrophy					I	I			
Ischemic heart disease		I	II A	II B	I 1	II C 2	II D		
Heart failure	II	I 3			I	II C 4	II	II	
Permanent atrial fibrillation		I		I					
Tachyarrhythmias		I							
Aortic aneurysm		I							
Peripheral arterial disease			I		I				
Previous stroke	I 5				II	I			
Metabolic syndrome			II	II	I	I			
Diabetes	II 5		II		I 6	I			
Patients with multiple cardiovascular and metabolic complications					I 6	II C 7			
Hyperuricaemia/gout					I	I			
Hypertension in the elderly	I		I		II	II			
Hypertension above 80 years of age	I 8				II				
Isolated systolic hypertension	I		I		II	II			
Albuminuria/ /proteinuria			II 9	II	I	I			
Diabetic/non-diabetic nephropathy					I	I			
Chronic kidney disease					I	I		II	
Pregnancy		II 10	II 11	II 12					I
Erectile dysfunction		II 13	II		I	I			
Asthma/chronic obstructive pulmonary disease			I			I			
Glaucoma		I							

I — first choice drug
II — second choice drug for combined treatment
A — with angina
B — with β-blocker intolerance
C — with angiotensin-converting enzyme inhibitor intolerance
D — after myocardial infarction
1 — preferred agents: perindopril, ramipril, zofenopril
2 — preferred agents: telmisartan and valsartan
3 — only carvedilol, bisoprolol, metoprolol XR/CR, nebivolol
4 — preferred agents: candesartan and valsartan
5 — preferred agent: indapamide
6 — preferred agents: perindopril, ramipril
7 — telmisartan has the first-choice status
8 — only indapamide
9 — preferred agent: lercanidipine
10 — preferred agent: labetalol (poor availability in Poland), of other β-blockers only metoprolol
11 — only nifedipine (extended release preparation preferred)
12 — only verapamil
13 — only nebivolol
TD — thiazide/thiazide-like diuretics
BB — β-blockers
CA-dhp — dihydropyridine calcium antagonists
CA-ndhp — non-dihydropyridine calcium antagonists
ACEI — angiotensin-converting enzyme inhibitors
ARB — angiotensin receptor blockers
AA — aldosterone antagonists
LD — loop diuretics
MD — methyldopa

*SPC should contain two first-choice drugs or one first-choice drug and one second-choice drug, except for not recommended combinations of ACEI + ARB and BB + CA-ndhp (SPC not available)

Tabela XXIII. Absolute and relative contraindications to specific antihypertensive drug classes

Drug class	Absolute contraindications	Relative contraindications
Thiazide diuretics	Gout	Metabolic syndrome
		Glucose intolerance
		Hyponatremia < 130 mmol/L
		Pregnancy
β-blockers	Asthma 2nd or 3rd degree atrioventricular block	Chronic obstructive pulmonary disease
		Metabolic syndrome
		Glucose intolerance
		Athletes and physically active patients
Dihydropyridine calcium antagonists		Tachyarrhythmias
		Heart failure
Non-dihydropyridine calcium antagonists (verapamil/diltiazem)	2nd or 3rd degree atrioventricular block	Chronic constipation (verapamil)
	Heart failure	
	Bradycardia < 50 bpm	
Angiotensin-converting enzyme inhibitors	Pregnancy	
	Hyperkalaemia > 5.0 mmol/L	
	Bilateral or single kidney renal artery stenosis	
	Transplant renal artery stenosis	
	History of angioneurotic oedema	
Angiotensin receptor blockers	Pregnancy	
	Hyperkalaemia > 5.0 mmol/L	
	Bilateral or single kidney renal artery stenosis	
Aldosterone antagonists	Chronic kidney disease (eGFR < 30 mL/min)	
	Hyperkalaemia > 5.0 mmol/L	
	Pregnancy	

bpm — beats per minute; eGFR — estimated glomerular filtration rate

medications in relation to the patient's age. However, as dictated by the clinical experience, and if there are no specific indications to individualise therapy otherwise, first-line drugs are thiazide/thiazide-like diuretics and dihydropyridine calcium antagonists, which may be used in monotherapy in grade 1 hypertension. The preferred SPC in uncomplicated hypertension in this age group is a combination of thiazide-type diuretic and dihydropyridine calcium antagonist, while patients with cardiovascular disease should receive an ACEI-containing SPC, and those after a coronary event should receive ACEI + β-blocker. The principles of antihypertensive therapy in the elderly patients are shown in Table XXIV, and the modified algorithm for the management of hypertension in patients aged 65-80 years is shown in Figure 6.

In patients above 80 years of age, available studies (HYVET) indicate that the therapy should be initiated with a long-acting thiazide-like diuretic (indapamid), with a possible addition of an ACEI, and in those with grade 3 hypertension, a respective SPC should be used. The modified algorithm for the management of hypertension in patients above 80 years of age is shown in Figure 7.

5.3. Isolated systolic hypertension in the elderly

Isolated systolic hypertension is defined as persistently elevated SBP (> 140 mm Hg) with normal DBP values (< 90 mm Hg). It a predominant form of hypertension in the elderly patients. The pathogenesis of this type of hypertension has been well defined and is related to reduced large elasticity and compliance of the aorta and other large arteries due to age- and atherosclerosis-related calcium and collagen deposition, replacing elastin in the large artery walls. Due to these changes, the capacitance function of the aorta is reduced, leading to an increase in SBP and a decrease in DBP.

Table XXIV. Antihypertensive treatment strategies in the elderly

In patients aged 65–80 years, regardless of hypertension grade, initiation of antihypertensive therapy according to the general principles is recommended
In patients aged 65–80 years, target BP < 140/90 mm Hg is recommended if the treatment is well tolerated but BP should not be lowered below 130/70 mm Hg
In patients > 80 years of age with grade 2–3 hypertension, drug therapy to reduce SBP to 140–150 mm Hg is recommended, provided the patient is in a good physical and mental condition
In patients who reach 65 or 80 years of age, continuation of previous well-tolerated antihypertensive therapy should be considered regardless of achieved/target BP values
In patients > 80 years of age with grade 1 hypertension, drug therapy is not recommended
In the elderly, initial drug doses should be lower, and subsequent therapy intensification should be more cautious due to a higher risk of adverse effects (hypotension). Monotherapy is acceptable in patients aged 65-80 years with grade 1 hypertension and patients > 80 years of age with grade 2 hypertension
All major drug classes may be used for monotherapy, with some preference for dihydropyridine calcium antagonists and thiazide-like diuretics. SPC may contain drugs from these two classes or one of these drugs and ACEI or ARB
In the elderly with isolated systolic hypertension, the preferred drugs are thiazide/thiazide-like diuretics, dihydropyridine calcium antagonists, and SPC containing one of these drugs and ACEI or ARB
In patients > 80 years of age, the preferred first line drug is indapamide, combined with ACEI in SPC

ACEI — angiotensin-converting enzyme inhibitor; ARB — angiotensin receptor blocker; BP — blood pressure; SBP — systolic blood pressure; SPC — single pill combination

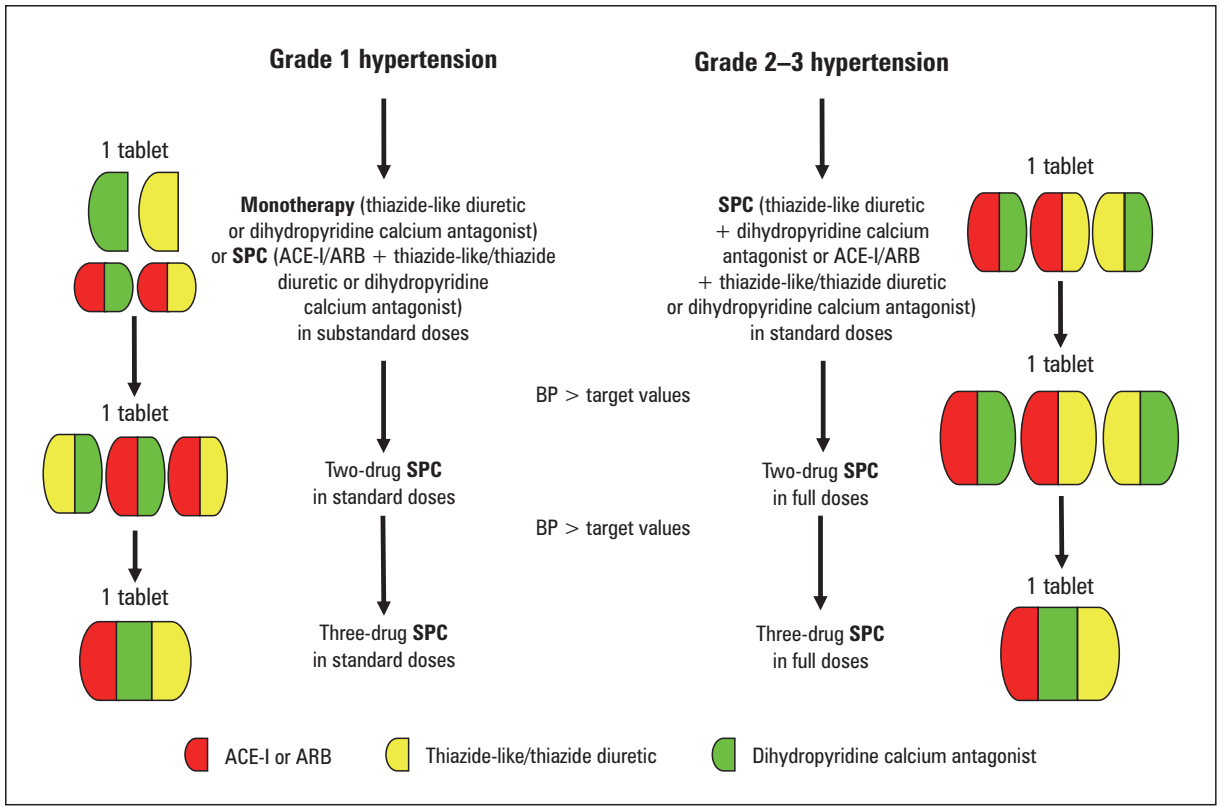


Figure 6. Algorithm for antihypertensive drug therapy in patients with hypertension aged 65-80 years. ACEI — angiotensin-converting enzyme inhibitor; ARB — angiotensin receptor blocker; BP — blood pressure; SPC — single pill combination

While SBP is the major determinant of cardiovascular risk, reduced DBP is a pathophysiological determinant of the so-called J-curve, or an increase in ischaemic heart disease risk with excessive DBP lowering. This has therapeutic implications, as efforts to reduce SBP are associated with a risk of excessive DBP lowering, and it has been reflected in the recommendations on target BP values in this type of

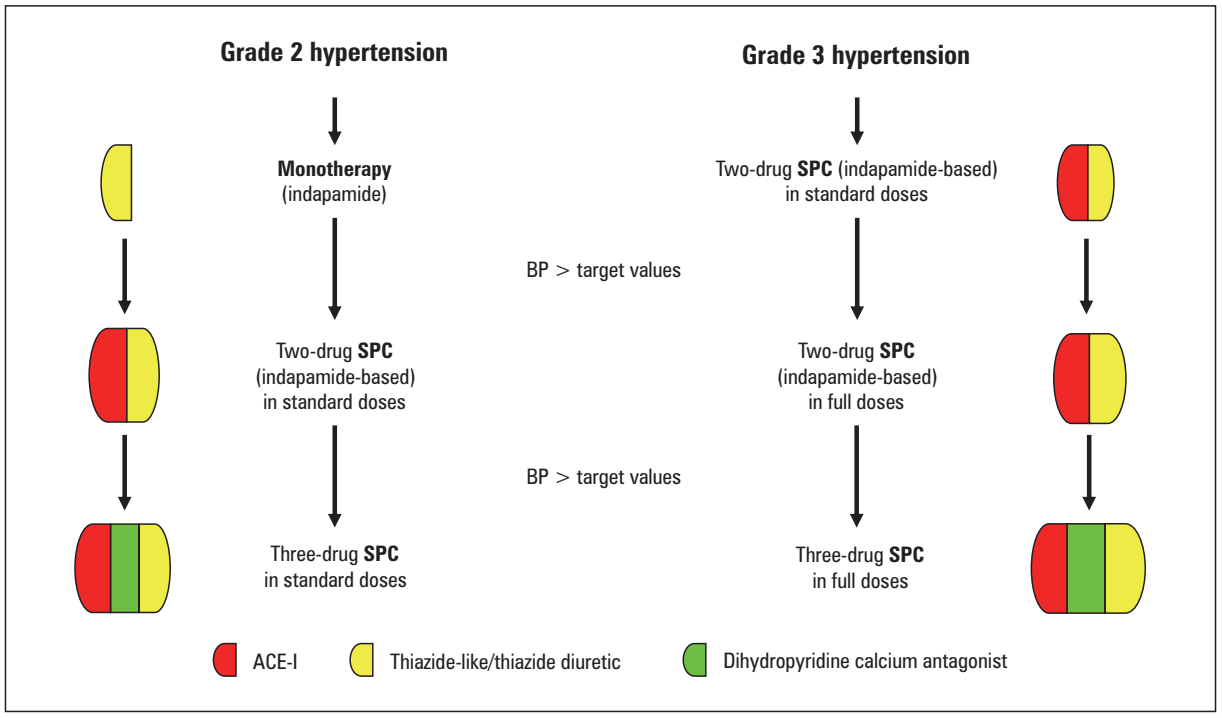


Figure 7. Algorithm for antihypertensive drug therapy in patients with hypertension aged > 80 years. ACEI — angiotensin-converting enzyme inhibitor; ARB — angiotensin receptor blocker; BP — blood pressure; SPC — single pill combination

hypertension (SBP should be lowered according to the general recommendations for specific age groups but DBP should not be lowered below 65 mm Hg). It should be remembered that antihypertensive agents induce proportional lowering of both SBP and DBP and despite some differences between them, they cannot rapidly affect aortic compliance which determines SBP elevation with concomitant DBP reduction.

In patients with ISH, thiazide/thiazide-like diuretics and dihydropyridine calcium antagonists are preferred, possibly with an addition of a RAS inhibitor. This recommendation stems from the three clinical trials in patients with this type of hypertension (SHEP, Syst-Eur, HYVET).

5.4. Hypertension in women

In the Blood Pressure Lowering Treatment Trialists' Collaboration metaanalysis that compared benefits of antihypertensive therapy in men and women, both similar BP-lowering effect and similar treatment outcomes were noted in both genders, with no differences in response to different classes of antihypertensive medications.

Hypertension management in women of reproductive age, during pregnancy, and in the postpartum period has been discussed in a separate expert consensus statement of the Polish Society of Hypertension (PTNT), the Polish Cardiac Society (PTK), and the Polish Society of Gynecologists and Obstetricians (PTGP). The basic management principles are summarised in Tables XXV and XXVI.

Among the 5 major antihypertensive drug classes, calcium antagonists (preferably dihydropyridines) and/or β-blockers should be considered in women of reproductive age. Thiazide/thiazide-like diuretics may also be considered but these should be withdrawn during pregnancy. In hypertensive women planning pregnancy, a choice of a β-blocker which may be later continued during pregnancy if required should be considered (e.g., metoprolol). Basic two-drug combinations which may be used in women of reproductive age include dihydropyridine calcium antagonist + β-blocker and calcium antagonist + thiazide/thiazide-like diuretic (SPC are available that contain these combinations).

In women of reproductive age, substituting drugs typically used during pregnancy for regular chronic antihypertensive therapy may be considered already when planning pregnancy (particularly labetalol and extended-release nifedipine, if these drugs were available in Poland in the future). Use of drugs recommended during pregnancy may also be considered in women in whom use of assisted reproduction technology is planned.

Table XXV. Antihypertensive treatment strategies in women of reproductive age, during pregnancy and in the postpartum period, based on the PTNT/PTK/PTGP expert consensus statement (part 1)

In all women of reproductive age, lifestyle changes are recommended, in particular smoking cessation, limitation of alcohol intake, and body weight reduction
In hypertensive women of reproductive age, β-blockers and/or calcium antagonists should be considered
In hypertensive women of reproductive age, thiazide/thiazide-like diuretic may be considered
In women of reproductive age, substituting drugs typically used during pregnancy for regular chronic antihypertensive therapy may be considered already when planning pregnancy
Substituting drugs typically used during pregnancy for regular chronic antihypertensive therapy may be considered in women in whom use of assisted reproduction technology is planned.
During pregnancy, hypertension should be diagnosed if SBP is ≥ 140 mm Hg and/or SBP is ≥ 90 mm Hg in office measurements, confirmed by out-of-office measurements within 7 days in the first trimester and up to 2–3 days in the second and third trimester.
In pregnant women, it is recommended to maintain BP in the 110–140/80–85 mm Hg range
If SBP is ≥ 160 mm Hg and/or DBP is ≥ 110 mm Hg and/or symptoms are present that may suggest development of preeclampsia, it is recommended to refer the patient to a hospital

BP — blood pressure; DBP — diastolic blood pressure; SBP — systolic blood pressure

Table XXVI. Antihypertensive treatment strategies in women of reproductive age, during pregnancy and in the postpartum period, based on the PTNT/PTK/PTGP expert consensus statement (part 2)

In pregnant women with hypertension, first-line drugs include methyldopa, labetalol and extended release nifedipine
If a cardioselective β-blocker is indicated in pregnant women with hypertension, metoprolol should be considered
It is not recommended to use ACEI, ARB, renin inhibitors, and diltiazem during pregnancy (except for special clinical situations)
It is not recommended to use diuretics and spironolactone during pregnancy (except for special clinical situations)
Drugs indicated for emergency treatment of hypertension during pregnancy include intravenous labetalol, oral nifedipine, and intravenous hydralazine
The recommended rate of BP lowering during emergency treatment of hypertension it to reduce mean arterial pressure by not more than 25% during minutes/hours
In lactating women, use of labetalol or metoprolol or extended release nifedipine (or amlodipine) should be considered. Substituting other antihypertensive drugs for methyldopa should also be considered
In lactating women, use of ACEI, ARB, and diuretics is not recommended
In women at a high risk of preeclampsia (e.g., women with chronic hypertension or gestational hypertension during previous pregnancy), acetylsalicylic acid 100–150 mg once daily in the evening is recommended. The treatment should be started before 16 weeks of gestation and continued until 36 weeks of gestation

ACEI — angiotensin-converting enzyme inhibitor; ARB — angiotensin receptor blocker; BP — blood pressure

In women of reproductive age, ACEI, ARB, renin inhibitors, and mineralocorticoid receptor antagonists should not be used due to potential teratogenic effects of these drugs.

Hypertension is not an absolute contraindication for the use of hormonal replacement therapy or oral contraception. If these therapies are used, BP should be measured at each visit and hypertension should be treated according to the general management principles.

The likelihood of BP increase in hypertensive women who receive hormone replacement therapy during menopause is small, but hormone replacement therapy and selective oestrogen receptor modulators should not be used for primary or secondary prevention of cardiovascular events.

Use of oral contraceptives is associated with a small but significant BP increase and development of hypertension. However, most studies evaluated the effect of older generation contraceptives that contained a higher oestrogen dose than those currently used. Data are lacking regarding the effect of newer hormonal contraceptive methods (vaginal and transdermal) on BP but an association was confirmed between newer contraceptive methods and an increased risk of venous thrombosis. Progestin-only containing oral contraceptives (minipills) are not considered contraindicated in mild and moderate hypertension but they constitute a minor proportion of currently used oral contraceptives.

5.5. Hypertension in pregnant women

Taking into account pathophysiological, clinical picture, and management differences, the PTNT/ /PTK/PTGP expert consensus statement has divided hypertension during pregnancy into two major types:

- chronic (preexisting) hypertension: present before pregnancy or developing before 20 weeks of gestation and persisting usually beyond 6 or more weeks after delivery, which may be further subcategorised as:
  — primary hypertension;
  — secondary hypertension.
- gestational (pregnancy-induced) hypertension: developing after 20 weeks of gestation and usually resolving within 6 weeks after delivery, which may be further subcategorised as:
  — gestational hypertension;
  — preeclampsia.

Preeclampsia is a complication of placental dysfunction, and thus it develops mostly in the second half of pregnancy in pregnancy-induced hypertension but may also occur in women with preexisting hypertension, in whom BP elevation with other features of preeclampsia are seen after 20 weeks of gestation — this should be diagnosed as **preeclampsia superimposed upon chronic hypertension**.

Other serious complications of hypertension in pregnancy include the **HELLP syndrome** (clotting abnormalities, hepatic dysfunction, and low platelet count) and **eclampsia** or development of central nervous system dysfunction symptoms.

The principles of hypertension management in pregnant women, which have been discussed in detail in the above mentioned PTNT/PTK/PTGP expert consensus statement, are summarised in Tables XXV and XXVI.

5.6. Hypertension in patients with metabolic syndrome

Hypertension or high normal BP is a frequent component of metabolic syndrome. Recommending lifestyle changes, particularly body weight reduction and increased physical activity, is very important in all individuals with metabolic syndrome as the first and foremost intervention in the management of hypertension. The aim is to reduce body weight by 7–10% over 6–12 months by modest reduction of caloric intake (by 500–1000 kcal per day) which is usually more effective than a more rigorous diet.

Indications for initiating drug therapy and target BP values do not differ from the general principles of antihypertensive therapy considering the patient's age. Currently, no evidence from outcome trials justifies initiation of drug treatment in patients with metabolic syndrome and high normal BP. Metabolic syndrome is associated with a high risk of developing diabetes, and thus the effect of antihypertensive drugs on glucose metabolism and the risk of new-onset diabetes which was evaluated in many clinical trials should be taken into consideration when choosing antihypertensive drug classes. Drug therapy should be initiated with RAAS inhibitors which delay development of diabetes, combined with a calcium antagonist or a thiazide-like diuretic and administered as SPC, or even a three-drug SPC if required. β-blockers and conventional thiazide diuretics should be avoided in patients with metabolic syndrome. If drugs from these classes are indicated, vasodilating β-blockers and thiazide-like diuretics should be chosen. When prescribing a diuretic, a potassium-sparing preparation may be considered, as hypokalaemia worsens glucose tolerance.

5.7. Hypertension in diabetic patients

The prevalence of hypertension among diabetic patients is increased compared to the general population. Masked hypertension is often present in diabetic patients, in particular nocturnal hypertension and a non-dipping circadian BP pattern. Another relatively frequent phenomenon is orthostatic hypotension due to autonomic neuropathy which is typical for diabetes. Thus, ABPM is recommended in each diabetic patient. BP should also be measured in the standing position in case of symptoms suggesting hypotension during therapy intensification.

Blood pressure lowering brings documented benefits in regard to the reduction of mortality risk and the rates of all cardiovascular and renal complications (except for diabetic neuropathy). These benefits are greater and more lasting compared to benefits from good blood glucose control. In patients with hypertension and diabetes, antihypertensive drug therapy is typically recommended when BP is > 140/90 mm Hg. No evidence is available from outcome clinical trials that would justify initiating drug therapy in patients with diabetes and high normal BP, although use of a RAAS inhibitor in a substandard to standard dose is justified if micro- or macroalbuminuria is identified. Following the 2018 ESC/ESH guidelines, we recommend target BP values in diabetes as in the general population of hypertensive patients, considering the patient's age. This is mostly justified by the nephroprotective effect of antihypertensive treatment, although the SPRINT trial did not include diabetic patients, and the earlier 2012 ESH/ESC guidelines indicated that the optimal reduction of the global cardiovascular

risk in most patients with hypertension and diabetes was obtained by lowering BP below 140/85 mm Hg. This target DBP value was based on an analysis of HOT and UKPDS study findings, and in turn, benefits of SBP lowering below 130 mm Hg in diabetic patients have not been confirmed in the ACCORD and INVEST studies.

Effective BP control in diabetic patients is difficult. Due to a proven nephroprotective effect of RAAS inhibitors, ACEI or ARB should be an invariable component of SPC. When choosing between ACEI and ARB in diabetic patients, results of the most recent metaanalysis of studies performed in this group of patients may be taken into consideration, showing a greater long-term cardioprotective effect of ACEI. For combined therapy, first choices should include a RAAS inhibitor with a calcium antagonist (ACCOMPLISH) or a thiazide-like diuretic (ADVANCE). The ADVANCE ON study results showed for the first time that antihypertensive therapy using a SPC (perindopril + indapamide) may yield long-term (10 years) outcome benefits in terms of a reduction of cardiovascular and all-cause mortality.

Concomitant administration of two RAAS inhibitors (also including the renin inhibitor) should be avoided due to a higher risk of hyperkalaemia and worsening of renal function (ONTARGET and ALTITUDE studies).

The management of patients with hypertension and diabetes should be particularly targeted at improvement of all cardiovascular risk factors. This means a strong indication for a statin, while acetylsalicylic acid (ASA) should not be used for primary prevention. The basic principles of the management of hypertension in diabetic patients are shown in Table XXVII.

A growing role of SGLT2 inhibitors (empagliflosine, kanagliflosine, dapagliflosine) should be acknowledged, as these drugs improve cardiovascular outcomes, reduce the risk of heart failure, and show a clear BP-lowering effect in patients with diabetes.

5.8. Hypertension in patients with chronic kidney disease

Observational studies show a direct correlation between BP values and development of chronic kidney disease. Protection from further progression of renal disease requires strict BP control and reducing proteinuria as much as possible, while the effect of reducing albuminuria on the reduction of cardiovascular risk is not clear. Despite many studies and metaanalyses on optimal target BP in this patient group, due to discordant conclusions from these analyses it seems reasonable to recommend target BP values as in the general population of hypertensive patients, considering the patient's age (Table II). Lowering BP below 120/80 mm Hg to delay albuminuria is questionable (ROADMAP study), and in patients with hypertension and concomitant nephropathy with large proteinuria, this decision remains a domain of nephrologists.

Dietary salt restriction is a particularly important non-drug measure in these patients. Compared to other classes of antihypertensive medications, ACEI and ARB are more effective at reducing proteinuria and delaying progression of renal disease, and thus are indicated in patients with moderately reduced glomerular filtration rate and/or proteinuria. Therapy should be started with low doses that are later cautiously increased to moderate ones, with eGFR and potassium level monitoring. Reduction of baseline eGFR by 10–20% during the first 4–12 weeks of therapy should be considered acceptable. ACEI and ARB should not be used in patients with acute kidney injury, and initiation of these drugs is not recommended, unless supervised by a nephrologist, in patients with chronic kidney disease and eGFR below 30 mL/min/1.73 m^2.

Table XXVII. Antihypertensive treatment strategies in patients with diabetes

Immediate drug therapy is recommended in patients with hypertension, and in those with high normal BP only if proteinuria is present
Target BP in patients with diabetes is < 130/80 mm Hg but specific BP targets in various age groups should be taken into account
The presence of proteinuria does not modify target BP
In diabetes, the preferred drugs are RAAS inhibitors (ACEI and ARB) due to a greater nephroprotective effect
The therapy is initiated with an SPC containing a RAAS inhibitor and dihydropyridine calcium antagonist or diuretic (thiazide-like agents are preferred)
If a β-blocker is required (due to cardiac disease), vasodilating agents seem more beneficial (due to a more favourable metabolic profile)
It is not recommended to combine two RAAS inhibitors
Statin therapy is recommended in diabetic patients
Acetylsalicylic acid is not recommended in diabetic patients without cardiovascular disease

ACEI — angiotensin-converting enzyme inhibitor; ARB — angiotensin receptor blocker; BP — blood pressure; RAAS — renin-angiotensin-aldosterone system; SPC — single pill combination

Combined antihypertensive therapy, optimally using SPC, is required to reach target BP values. Based on the results of the ACCOMPLISH study, it was shown that a combination of an ACEI with a calcium antagonist rather than a thiazide diuretic is more effective at preventing doubling of serum creatinine level and development of end-stage renal disease. The type and dose of a diuretic should be adjusted to renal function. Thiazide and thiazide-like diuretics should not be used in patients with eGFR below 30 mL/min, and loop diuretics should be used instead. Doses of loop diuretics should be increased with worsening of renal function.

In advanced chronic kidney disease, mineralocorticoid receptor antagonists are not recommended, particularly in combination with a RAS inhibitor, due to a risk of renal function worsening and development of hyperkalaemia. If mineralocorticoid receptor antagonists are used in this patient group, strict potassium level monitoring is required. Combining two RAS inhibitors is also not recommended despite potentially higher effectiveness in reducing proteinuria. The latter two therapeutic options should remain a domain of nephrologists.

5.9. Hypertension in patients after solid organ transplantation

Hypertension is present in most patients after solid organ transplantation. These patients often show lack of nocturnal BP dipping or even a reverse dipper circadian BP profile. For these reasons, ABPM is particularly indicated in patients after solid organ transplantation.

The major causes of hypertension in patients after solid organ transplantation include use of BP elevation-inducing immunosuppressive drugs (glucocorticosteroids and calcineurin inhibitors: ciclosporin A and tacrolimus) and renal dysfunction. Use of ciclosporin A is associated with a higher degree of BP increase compared to tacrolimus use. Reversible vasospasm is the major mechanism of the pressor effect of calcineurin inhibitors. This particularly involves renal afferent arterioles, leading to a reduction of the glomerular filtration rate and to renal interstitial ischaemia. The management of hypertension may include all regular lifestyle modifications and use of all antihypertensive drug classes. In view of the mechanism of the pressor effect of calcineurin inhibitors, dihydropyridine calcium antagonists should be preferred that have no effect on blood calcineurin inhibitor levels (nitrendipine, isradipine, lacidipine) or induce only slight elevation of these levels (amlodipine).

5.10. Hypertension complicated by ischaemic heart disease

Hypertension is an important factor in the pathogenesis of ischaemic heart disease (accelerated atherosclerosis, left ventricular hypertrophy), responsible for 25% of its total risk. Each BP lowering by 10 mm Hg reduces the risk of ischaemic heart disease by 17% regardless of baseline cardiovascular risk and the type of antihypertensive treatment used.

In hypertension with concomitant ischaemic heart disease, however, there is evidence suggesting existence of the J curve, or an increase in the coronary event risk with BP lowering below certain threshold. Two analyses suggested that SBP above 140 mm Hg and DBP above 80 mm Hg was associated with an increased risk of coronary event, but a similar increase in risk was seen for SBP below 120 mm Hg and DBP below 70 mm Hg. For this reason, both the recommended target BP values and undesirable levels of BP reduction are the same as in uncomplicated hypertension.

Although optimal BP reduction is the most important factor for the reduction of ischaemic heart disease risk, the recommended antihypertensive drugs in patients with established ischaemic heart disease are ACEI (preferred drugs of this class are perindopril — EUROPA study, ramipril — HOPE study, and zofenopril — SMILE 4 study) and β-blockers (preferred drugs of this class are bisoprolol, due to cardioselectivity and effecting heart rate lowering, and nebivolol, due to cardioselectivity and nitric oxide generation), particularly in patients after a myocardial infarction. As the recommendation for using SPC as the first-line therapy is valid also in these patients, it should be noted that the combination of bisoprolol and perindopril is the only SPC available in Poland than contains drugs from both preferred classes. If angina is present, calcium antagonists are also used. In patients with concomitant ischaemic heart disease, ARB are second-line drugs (preferred choices are telmisartan — ONTARGET study, and in patients after a myocardial infarction also valsartan — VALIANT study) in case of ACEI intolerance in patients with ischaemic heart disease, based on the results of multiple metaanalyses that compared these two drug classes in regard to the reduction of mortality and cardiac event risk.

It should be noted that the recommendations regarding drug therapy of stable coronary artery disease may be significantly modified in the future. This is related to new data regarding antiplatelet therapy regimens, new target LDL cholesterol levels, and introduction of the new term "chronic coronary syndromes" to replace the previous term "stable coro-

nary artery disease". These changes are expected to take place in Europe in 2019.

In this patient group, a particular role is played by so-called hybrid SPC [antihypertensive drug(s) + statin] which are discussed in the section on lipid-lowering therapy.

5.11. Hypertension complicated by heart failure

Along with ischemic heart disease, hypertension is one of the two major causes of heart failure. It often leads to left ventricular diastolic dysfunction and heart failure with preserved ejection fraction, in contrast to heart failure due to a previous coronary event, which is often associated with left ventricular systolic dysfunction and reduced ejection fraction. In both types of heart failure, hypertension is the most important modifiable risk factor for the development or progression of heart failure, and thus preventing heart failure involves use of antihypertensive drugs. Diuretics, β-blockers, ACEI, and ARB were shown to be beneficial, while calcium antagonists are not recommended.

In advanced heart failure, hypertension becomes less problematic due to reduction of cardiac output in this condition, and higher BP values are prognostically favourable.

Indications for initiating antihypertensive therapy and target BP values are the same as in uncomplicated hypertension, but any antihypertensive therapy should be undertaken with consideration of the current guidelines on the management of heart failure and the duration of the antihypertensive effect of specific drugs, which means that the preferred drugs in this patient group are β-blockers (only carvedilol, bisoprolol, metoprolol XR/CR, and nebivolol), ACEI (drugs studied in postinfarction left ventricular dysfunction include lisinopril, ramipril, trandolapril, and zofenopril), and aldosterone antagonists (eplerenone is the preferred drug). ARB are second-choice drugs in case of ACEI intolerance (preferred drugs of this class are candesartan and valsartan).

Diuretics are recommended in patients with clinical evidence of left- or right-sided heart failure. The preferred drugs are thiazide-like diuretics with greater natriuretic effect (chlorthalidone) and loop diuretics, which induce an even stronger natriuretic effect (preferred torasemide). Among the latter, torasemide is characterised by greater bioavailability, better absorption, and longer half-life compared to furosemide, and exerts an additional anti-aldosterone effect, which translated to increased clinical benefits observed in the non-randomised TORIC study.

5.12. Hypertension complicated by atrial fibrillation

Hypertension (and even high normal BP) predisposes to the development of atrial fibrillation. Due to frequent presence of asymptomatic atrial fibrillation in hypertensive patients, this arrhythmia should be actively searched for in this patient population. It has been estimated that atrial fibrillation is present in about 500,000 people in Poland. In this population, hypertension is present in nearly 80% of subjects. It is thus believed that hypertension is a major underlying factor in the vast majority of patients with atrial fibrillation. Hypertension leads to left ventricular hypertrophy and overload, increased left atrial volume and wall tension, and activation of the RAAS and the sympathetic nervous system, all resulting in electrical, structural, and neurohormonal remodeling of cardiomyocytes, which is a substrate for atrial fibrillation.

Major diagnostic and therapeutic challenges in this patient group include difficulties in diagnosing hypertension in patients with persistent and permanent atrial fibrillation, decisions regarding initiation of anticoagulant therapy, and antihypertensive therapy in patients w hypertension and atrial fibrillation.

Atrial fibrillation is a frequent cause of errors in BP measurement. The arrhythmia is associated with varying left ventricular filling times and stroke volume, which results in a large variability of BP values and low reproducibility of BP measurements. These limitations also hold true for ABPM. In this patient population, caution should be exercised when diagnosing hypertension based on only HBPM or ABPM, despite a class I recommendation for these methods for the diagnosis of hypertension in the ESC/ESH guidelines. Precise ascertainment of BP values in patients with atrial fibrillation is very important as it often underlies the decision to initiate anticoagulation. If BP is > 140/90 mm Hg in two measurements during at least two visits or the patient receives antihypertensive therapy, anticoagulation should be considered even if there are no other risk factors for thromboembolism (class IIa recommendation). Individual patient characteristics and preferences should also be taken into account. In these case, the criteria for the diagnosis of hypertension according to the European guidelines should be followed. If hypertension is accompanied by other risk factors for stroke including heart failure, age 65 years or above, vascular disease, diabetes, female gender, and a history of stroke/TIA, anticoagulation should be started (class I recommendation). When initiating anticoagulation, non-vitamin K oral anticoagulants (NOAC), including apixaban,

dabigatran, rivaroxaban and edoxaban (the latter not available in Poland), are preferred over warfarin and acenocoumarol. No data are available to indicate an advantage of any particular NOAC over the others in patients with hypertension. Renal function should be monitored during treatment with NOAC. Hypertension is not only an important risk factor for thromboembolic complications in patients with atrial fibrillation but also the most important modifiable risk factor for bleeding in patients with atrial fibrillation receiving anticoagulant therapy, particularly if SBP is above 160 mm Hg. Prevention of bleeding complications in this patient population involves careful BP control with values below 140/90 mm Hg, and preferably below 130/80 mm Hg. In most patients with hypertension and atrial fibrillation, the latter is associated with a rapid ventricular rate and β-blockers or non-dihydropyridine calcium antagonists (verapamil, diltiazem) are recommended. When choosing a β-blocker, the effect on slowing conduction at the atrioventricular junction should be taken into account, and this bisoprolol might be more beneficial than vasodilating β-blockers. Of note, SPC are available (β-blocker + other antihypertensive drug) that allow both BP and ventricular rate control. Non-dihydropyridine calcium antagonists are not recommended in patients with impaired left ventricular systolic function.

In those patients, β-blocker should be used for effective ventricular rate control, with digoxin added if required. In patients with hypertension, left ventricular hypertrophy, and high cardiovascular risk, RAAS inhibitors delay occurrence of the first atrial fibrillation episode, but these drugs do not prevent arrhythmia recurrence in patients with paroxysmal or persistent atrial fibrillation. In patients with atrial fibrillation, the choice of antihypertensive therapy is also determined by concomitant conditions such as coronary artery disease, heart failure, diabetes, chronic kidney disease, advanced age, and obesity. The choice of the therapy may also be dictated by further therapeutic plans regarding the management of arrhythmia itself. With higher recommendation class and increasing availability of electrophysiological procedures (ablation of the atrial fibrillation substrate), the importance of antiarrhythmic drugs (amiodarone, propafenone, sotalol) used to control ventricular rate is decreasing. Propafenone should not be used in patients with severe organic heart disease, while sotalol should not be used in patients with left ventricular hypertrophy, and verapamil and diltiazem should not be used in those with reduced left ventricular ejection fraction.

In summary, asymptomatic atrial fibrillation should actively searched for in patients with hypertension.

Anticoagulation with the preference of NOAC should be considered in all patients with hypertension and atrial fibrillation.

The management of hypertension in patients with concomitant atrial fibrillation is consistent with the general principles for hypertensive patents. Effective BP control in patients with atrial fibrillation receiving anticoagulant therapy prevents both ischaemic and haemorrhagic strokes. SPC containing a β-blocker and another antihypertensive drug should be preferred.

High bleeding risk is not a contraindication for anticoagulation but risk factors for bleeding should be reduced (BP control, time in therapeutic range > 70% when using vitamin K antagonists, avoidance of non-steroidal anti-inflammatory and antiplatelet drugs, limiting alcohol intake).

The basic principles of the management of hypertension in patients with cardiac complications are shown in Table XXVIII.

5.13. Hypertension and prevention of stroke

Regardless of the type of therapy, effective BP lowering reduces stroke risk more effectively than the risk of ischaemic heart disease. Metaanalyses indicate, however, that β-blockers are less effective and calcium antagonists are more effective at reducing stroke risk compared to other antihypertensive drug classes, although the data for β-blockers are based on atenolol and not modern cardioselective β-blockers, let alone the vasodilating ones.

Within 1–2 weeks (several days according to the 2018 ESC/ESH guidelines) after a stroke, and earlier after a TIA, BP normalisation should be sought according to the general management principles (target BP < 130/80 mm Hg should be reached slowly, and provided that treatment is well tolerated). The reported data indicate efficacy of thiazide-like diuretics (indapamide in the PATS study and combined with perindopril in the PROGRESS study) and ARB (eprosartan in the MOSES study) in the secondary prevention of stroke, although target BP in all these studies was < 140/90 mm Hg. Results of a more recent study on lacunar strokes suggest benefits from BP lowering below 130/80 mm Hg. During each visit, BP should be measured in the standing position to avoid excessive BP falls.

The effect of antihypertensive drug therapy on the severity of vascular dementia has not been clearly documented. One metaanalysis suggested that antihypertensive treatment was associated with a 9% reduction in the risk of incident dementia and cognitive dysfunction.

Table XXVIII. Antihypertensive treatment strategies in patients with cardiac disease

Antihypertensive therapy is indicated in grade ≥ 1 hypertension, and target BP in patients with heart disease is < 130/80 mm Hg Due to a possibility of the J-curve effect, the recommendation to avoid BP lowering to < 120/70 mm Hg is particularly important in patients with ischaemic heart disease
In patients with high normal BP, antiihypertensive drugs used for the treatment of ischaemic heart disease/heart failure are recommended but without the need for achieving target BP values
Preferred antihypertensive drugs in patients with ischemic heart disease are ACEI and β-blockers, particularly after a myocardial infarction, and in patients with angina also calcium antagonists
Preferred antihypertensive drugs in patients with heart failure are ACEI and β-blockers, followed by aldosterone antagonists (preferred eplerenone), and diuretics with evidence of volume overload
In patients with ischemic heart disease and/or heart failure, ARB are alternative second choice drugs in case of ACEI intolerance
In patients with atrial fibrillation with rapid ventricular response, β-blockers or possibly non-dihydropyridine calcium antagonists are recommended as antihypertensive drugs
Every hypertensive patient with atrial fibrillation requires antithrombotic treatment, preferentially with a novel oral anticoagulant
Every hypertensive patient with heart disease requires statin and acetylsalicylic acid
In patients with a risk of *de novo* or recurrent atrial fibrillation, ACEI or ARB may be considered for antihypertensive drug therapy, and eplerenone may be considered in patients with concomitant heart failure

ACEI — angiotensin-converting enzyme inhibitor; ARB — angiotensin receptor blocker; BP — blood pressure

Due attention should also be paid to other basic elements of secondary stroke prevention, such as lifestyle modification and treating risk factors, anticoagulation, use of antiplatelet agents, and surgical treatment of carotid artery stenosis.

Results of few studies on antihypertensive therapy in the acute phase of stroke are equivocal. It is believed that regardless of the stroke type, BP should be lowered in the acute phase of stroke only if SBP exceeds 220 mm Hg and/or DBP exceeds 120 mm Hg, and the drug if choice in these circumstances is labetalol (or, if it is unavailable, intravenous agents with a medium duration of action). BP should be slowly reduced to values about 170–180/110 mm Hg. In the SCAST study, no significant effect of antihypertensive drug therapy in the acute phase of stroke was found on cardiovascular events, including recurrent stroke.

Fibrinolytic therapy may be used if BP is lower than 185/110 mm Hg. On the second day after stroke, antihypertensive therapy may be initiated if BP is higher than 180 and/or 120 mm Hg.

The basic principles of the management of hypertension in patients after a stroke are shown in Table XXIX.

5.14. Other concomitant conditions

5.14.1. Hypertension with sexual dysfunction

Erectile dysfunction is more common in hypertensives than in individuals with normal BP values. Sexual dysfunction impairs patients' quality of life and is considered an independent cardiovascular risk factor and an early marker of atherosclerosis. At the same time, sexual dysfunction developing during antihypertensive therapy is a significant factor that has a negative effect on treatment compliance and persistence.

Multiple studies showed that antihypertensive drug therapy using older generation diuretics and β-blockers increases the risk of erectile dysfunction in men. Compared to these drugs, newer antihypertensive drug classes, i.e. ARB and ACEI, have a neutral or even beneficial effect on erectile function. If a β-blocker is needed, nebivolol is preferred, as in

Table XXIX. Antihypertensive treatment strategies in stroke patients

Target BP in patients after a stroke or TIA is < 130/80 mm Hg or < 140/90 mm Hg depending on patient age. Target BP values should be reached slowly, about 2 weeks after the acute event, provided that the treatment is well tolerated
Antihypertensive drug therapy for the secondary prevention of stroke should be based on an ARB or a thiazide-like diuretic (indapamid) with a possible addition of an ACEI
Other major components of secondary prevention are indicated, such as lifestyle changes and treatment of risk factors, anticoagulant and antiplatelet treatment, and surgical treatment of carotid artery disease (if indicated)
In the acute phase of stroke, treatment of hypertension is indicated only for BP > 220/120 mm Hg

ACEI — angiotensin-converting enzyme inhibitor; ARB — angiotensin receptor blocker; BP — blood pressure; TIA — transient ischemic attack

contrast to conventional β-blockers, nebivolol exerts a vasodilatatory effect related to nitric oxide release. Several studies showed that nebivolol may have a less effect on erectile dysfunction in men.

5.14.2. Hypertension and chronic obstructive pulmonary disease

Concomitant presence of hypertension and COPD is associated with a significantly increased cardiovascular risk. No studies compared the effect of antihypertensive therapy using different drug classes on long-term outcomes in patients with concomitant COPD. However, the mechanism of action of some antihypertensive drug classes calls for caution when using ACEI (bradykinin-mediated mechanism, cough inducing bronchospasm) and β-blockers (bronchospasm, reduced lung ventilation parameters, attenuated effect of β-agonists). If a drug from the latter class is required, its choice must be carefully dictated by cardioselectivity or additional protective properties, and attention must be paid to the recommended dose to minimise the effect on lung ventilation parameters. Cardioselective β-blockers were found to reduce mortality among patients with COPD and concomitant cardiac disease. Fewer concerns are associated with diuretic use (an effect synergistic with that of COPD itself, resulting in metabolic alkalosis and hypokalaemia, similarly to glucocorticosteroids and β-agonists, thickening of bronchial secretions). Safe antihypertensive drugs in patients with COPD include calcium antagonists and ARB.

5.14.3. Hypertension and glaucoma

The recommendations for coexisting hypertension and glaucoma have not been changed compared to the 2015 PTNT guidelines. The safest antihypertensive drugs that are not associated with a risk of glaucoma incidence and progression are β-blockers.

Among the risk factors for glaucoma, in addition to high BP, an increasing attention has been paid to systemic hypotension which may lead to reduced perfusion of the optic disc and induce glaucoma lesions. It seems that systemic hypotension is a much more important risk factor for progression of visual field defects than hypertension. Thus, overly aggressive antihypertensive therapy may lead to progression of glaucoma. Most importantly, adverse effects of antihypertensive therapy include excessive nocturnal BP fall with secondary reduction of ocular perfusion. In patients with glaucoma, evening dosing of antihypertensive drugs is contraindicated unless ABPM shows very high BP values during the night.

5.14.4. Hypertension and gout

An antihypertensive agent that reduces hyperuricaemia is losartan (this might have been of an importance for cardiovascular risk reduction in the LIFE study), but due to short duration of action and low availability in SPC, this drug is no longer considered the preferred choice for antihypertensive therapy in patients with concomitant gout. There are no contraindications for other ARB, ACEI, and calcium antagonists in patients with hyperuricaemia. In contrast, use of drugs that increase serum acid level, mostly thiazide/thiazide-like diuretics and β-blockers, is not advised. Allopurinol use, previously reserved for chronic secondary prevention of gout attacks, has become more common in hypertensives at high cardiovascular risk with asymptomatic hyperuricaemia (see chapter 6.3, uric acid-lowering therapy).

5.14.5. Hypertension and benign prostatic hyperplasia

When treating hypertension in men with benign prostatic hyperplasia, the general principles of antihypertensive therapy in the elderly using major drug classes should apply, and the previous recommendation to initiate therapy with an α-blocker has been abandoned after the ALLHAT study. The decision to use an alpha1-adrenergic receptor antagonist to improve micturition should be made by an urologist, with consideration of uroselective drugs (e.g., tamsulosin) for better cardiac safety in patients on established antihypertensive therapy. Non-selective alpha1-blockers (e.g., doxazosin) are among useful fourth- and fifth-line antihypertensive drugs in resistant hypertension (ASCOT, PATHWAY-2).

5.14.6. Hypertension and psoriasis

The prevalence of hypertension in patients with psoriasis is increased compared to the general population, as it's resistance to treatment. The pathogenesis of hypertension in patients with psoriasis is related, among other factors, to systemic inflammation. β-blockers should be avoided in hypertensives with psoriasis and no concomitant ischaemic heart disease, as these drugs may worsen psoriasis.

5.14.7. Hypertension in the perioperative period

Grade 1 and 2 hypertension does not require postponing a surgical procedure. In contrast, surgery should be postponed, unless it is urgent, until BP normalisation in a patient with grade 3 hypertension. Preoperatively, it is not desirable to aim for full BP normalisation by intensifying previous therapy. Target BP values may be in the range of 140–160/ /90–100 mm Hg (due to an additional BP-lowering

effect of anaesthetics). However, large BP variation in the perioperative period should be avoided.

Previous antihypertensive drug therapy should be generally continued, with usual morning dose of most BP-lowering drugs. If possible, withholding diuretics 2–3 days before a major surgery should be considered (due to potential adverse effects related to fluid loss and hypokalaemia), and possibly also RAAS inhibitors on the day of the surgery (with the last dose taken on the day before the surgery). In the recent years, controversies have arisen around the use of β-blockers in the perioperative period. Potential benefits of these drugs are limited to patients with a history of myocardial infarction or with heart failure, and thus patient populations in which long-term use of β-blockers is indicated anyway. In other patients, initiating β-blocker therapy, particularly several days before the surgery, may be associated with an increased mortality risk. In the recent ESC guidelines, more consideration has been given to perioperative statin than β-blocker use.

5.14.8. Hypertension in cancer patients

Hypertension is the most common cardiovascular diagnosis in cancer patients, present in one in three patients in this population. This is related not only with the prevalence of hypertension in specific age groups but also with the use of two widely implemented anticancer drug classes: VEGF pathway inhibitors (bevacizumab, sorafenib, sunitinib, pazopanib) and proteasome inhibitors (carfilzomib). The former inhibit nitric oxide production in the arterial wall, and the latter reduce vasodilatatory response to acetylcholine, favoring vasospasm over vasodilation. BP increase is observed in up to 30% of patients treated with these drugs, often during the first months of therapy. In patients who developed hypertension and those with DBP increase by 20 mm Hg or more compared to pretreatment values, antihypertensive therapy should be initiated or intensified, and the preferred drugs are RAAS inhibitors and calcium antagonists.

Among the latter, dihydropyridines should be used, as the non-dihydropyridine agents (diltiazem, verapamil) block CYP3A4 isoenzyme which is involved in the metabolism of, e.g., sorafenib, which may increase blood level of the latter or even lead to its direct toxicity. Evidence from preclinical (captopril, perindopril, zofenopril) and clinical (perindopril) studies on anticancer activity of ACEI support not only safety and but also additional benefits of ACEI in the treatment of hypertension in cancer patients.

With advances in oncological treatment and a general outcome and survival improvement in many malignancies, chronic antihypertensive therapy, similarly to that in other patients with hypertension, should be preferably undertaken with newer drugs, free from some adverse effects that characterise the older drugs.

5.15. Resistant hypertension

The management algorithm in patients with suspected resistant hypertension is shown in Figure 8.

Resistant hypertension is defined as inadequate BP control (BP values persistently ≥140/90 mm Hg) during appropriate combination therapy with 3 drugs (including a diuretic) in adequate doses, confirmed by ABPM and after patient non-compliance has been excluded.

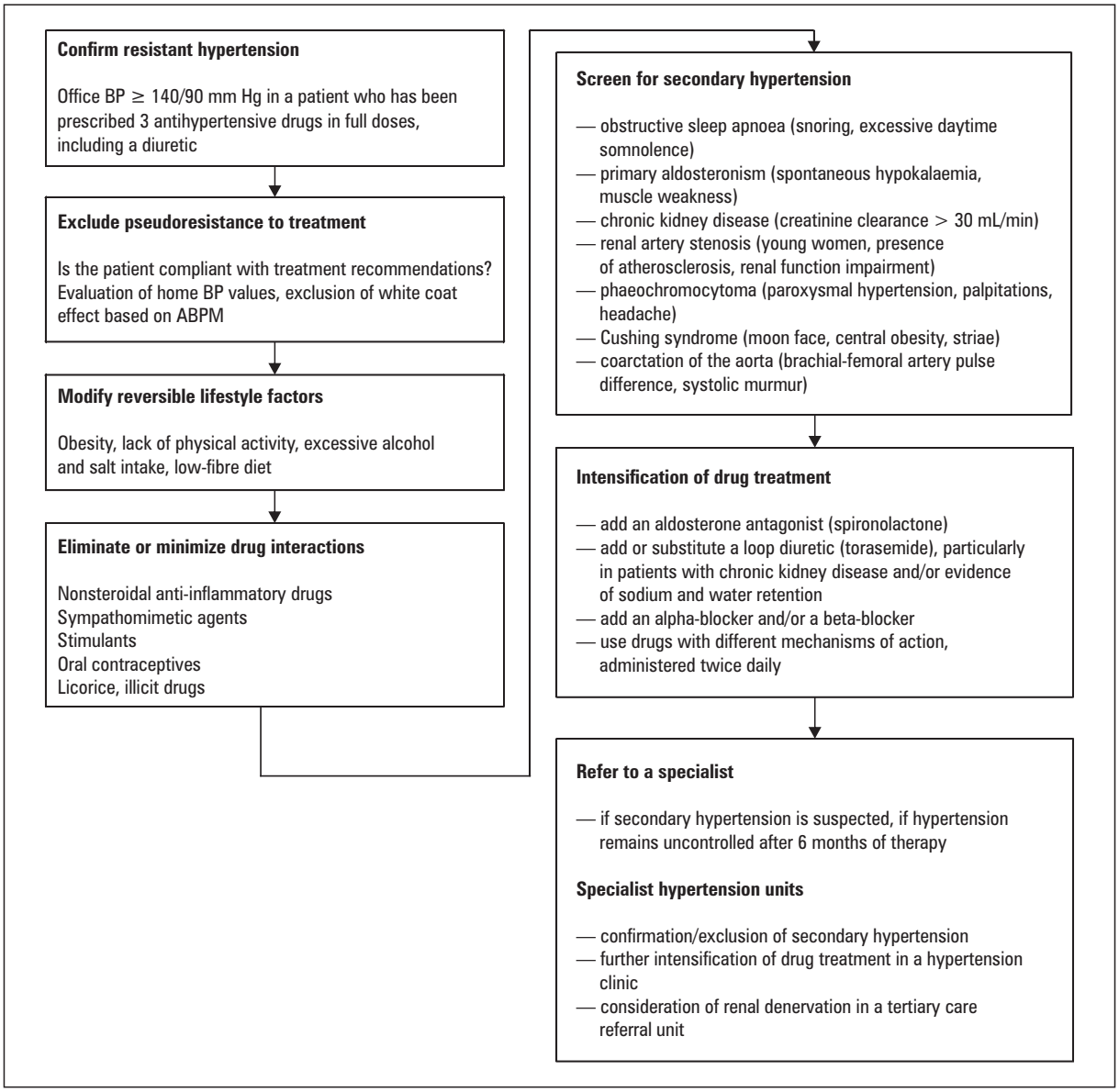
With this definition, resistant hypertension is a common clinical problem. Due to lowered target BP values (< 130/80 mm Hg), it is worth considering a change of this definition, with the new definition as follows: persistence of BP values ≥ target values for given patient age when using 4 drugs, including an aldosterone antagonist. This change has not been made in the present guidelines to retain consistency with the 2018 ESC/ESH guidelines. In Poland, the proportion of patients with resistant hypertension has been estimated at 10–13% of all treated hypertensives. With lower target BP values, this proportion would be higher. Patients with resistant hypertension are characterised by an increased cardiovascular risk compared to those with well controlled BP. Cardiovascular risk is also related to the number of antihypertensive drugs used.

Most commonly, pseudoresistance to treatment is observed due to the following reasons:

— non-compliance;
— inappropriate drug treatment — too low drug doses, drug combinations including no diuretic;
— BP increase in office measurements (white coat effect);
— errors during BP measurement;
— pseudohypertension.

The most common identifiable and often correctable reasons for treatment resistance include:

1. Lack of appropriate lifestyle modifications, including body weight increase and consumption of large amounts of alcohol.
2. Taking medications and substances that raise BP (e.g., non-steroidal anti-inflammatory drugs, glucocorticosteroids, cocaine, licorice etc.).
3. Undiagnosed secondary hypertension. Common causes include obstructive sleep apnoea, renal disease, primary hyperaldosteronism, and renal artery stenosis.
4. Volume overload due to inappropriate diuretic treatment, progressive renal dysfunction, and large sodium intake.



Rycina 8. Management algorithm in suspected resistant hypertension. BP — blood pressure

5. Advanced, irreversible vascular damage leading to a significant increase in the arteriolar wall-to-lumen ratio or reduced large artery compliance.

After excluding these often difficult-to-eliminate causes, the prevalence of true resistant hypertension is much lower. In patients with true resistant hypertension, SBP values are usually very high, and the prevalence of severe left ventricular hypertrophy and renal dysfunction is increased.

5.15.1. Drug therapy of resistant hypertension

The recommended and effective three-drug combination includes a RAAS inhibitor, thiazide/thiazide-like diuretic, and a calcium antagonist, preferably as a SPC. In some patients with resistant hypertension, changing previous medications to this three-drug combination may be associated with improved BP control. In resistant hypertension, a good response has been observed to a mineralocorticoid receptor antagonist as the next treatment step, particularly spironolactone, even in low doses of 25–50 mg/day. The PATHWAY-2 study showed that treatment with spironolactone was associated with a greater BP-lowering effect compared to bisoprolol or doxazosin use. If spironolactone is not tolerated, eplerenone may be used instead. BP lowering in response to administration of an aldosterone antagonist may be attributed to lowering aldosterone level, which is often elevated in resistant hypertension due to a re-increase in aldo-

Table XXX. Antihypertensive treatment strategies in patients with resistant hypertension

Pseudoresistance should be excluded, correctable causes of treatment resistance should be eliminated, and compliance should be confirmed before institution of additional therapy
In patients who are unsuccessfully treated with a RAAS inhibitor, thiazide-like/thiazide diuretic, and calcium antagonist in maximal doses, an aldosterone antagonist should be added (spironolactone 25–50 mg/d)
The next step should be to add or substitute a loop diuretic (torasemide 10–20 mg/d), particularly in patients with severe kidney dysfunction
The next step should be to add an α-blocker (doxazosin 4–8 mg/d) or a β-blocker (bisoprolol 5–10 mg/d). A vasodilating β-blocker may be considered (nebivolol 10 mg/d)
As the next step, addition of a direct arteriolar vasodilator (hydralazine) or a central acting agent (clonidine) should be considered
In exceptional cases of truly resistant hypertension, after all the above drug treatment measures have been tried, invasive treatment (renal denervation) may be considered
Patient selection for renal denervation should be a domain of hypertension specialists, and these procedures should be performed by invasive cardiologists in specialized centres

RAAS — renin-angiotensin-aldosterone system

sterone release following its initial reduction induced by RAAS inhibition, or due to unrecognised mild primary hyperaldosteronism. The next treatment step should be to use a loop diuretic, particularly torasemide, in addition to or instead of a thiazide/thiazide-like diuretic, with such substitution particularly in patients with renal dysfunction, and obligatorily in patients with eGFR < 30 mL/min/1.73 m^2. Further treatment intensification includes adding an alpha1-blocker (doxazosin) or a β-blocker (bisoprolol). In regard to the choice of a β-blocker, a vasodilating β-blocker may also be considered (nebivolol at the dose of 10 mg). Of note, some older generation antihypertensive drugs may be effective in the treatment of resistant hypertension, i.e., direct arterial vasodilators (hydralazine) and central sympatholytic drugs (clonidine). In resistant hypertension, twice daily dosing of antihypertensive drugs is frequently necessary.

The algorithm for the management of resistant hypertension is shown in Table XXX.

5.16. Renal artery ablation (renal denervation)

Experimental and clinical studies indicate that damage to afferent and efferent renal nerves has a beneficial effect on the pathophysiological mechanisms that contribute to the pathogenesis of hypertension, ultimately leading to BP lowering. Results of the pilot Symplicity HTN-1 study and the randomised Symplicity HTN-2 study showed that renal denervation was very effective at controlling BP in patients with resistant hypertension. However, based on the degree of renal denervation as evaluated by renal noradrenaline release, only partial (47%) effectiveness of the procedures was shown. The BP-lowering effect of renal denervation was questioned after publication of the large Symplicity HTN-3 study results, conducted in the United States in patients with resistant hypertension who were randomised to renal denervation or a sham procedure. At 6 months of follow-up, no significant difference in BP lowering was seen between the groups. A careful analysis of the study protocol and conduct showed many significant limitations of this study (e.g., inadequate experience in performing renal denervation, as indicated by the fact that 111 operators were performing these procedures in 88 centres in the United States, modification of antihypertensive drug therapy in 40% of patients before the primary endpoint was analysed, incomplete renal artery ablation in 70% of the treated patients, and no methods to verify the effectiveness of renal denervation) which are believed to contribute significantly to no difference in SBP between the study group and the control group. At the same time, autopsy studies were published which showed a large interindividual variation of renal innervation and a higher effectiveness of those procedures which involved the whole vessel circumference, main renal arteries including the distal part of the artery with its branches, and accessory renal arteries, which may be challenging in terms of the available renal ablation catheters and their size in relation to the vessel size. The randomised PRAGUE-15 study showed that renal denervation is equally effective at lowering BP as adding spironolactone but a subanalysis of this study showed that 39% of patients did not tolerate spironolactone treatment, and this proportion is higher compared to the usually reported rates of adverse effects during this treatment (10–30%). Another randomised DENERHTN study showed an advantage of renal denervation in terms of BP reduction (by 5.9 mm Hg) in patients with resistant hypertension compared to the control group, with the same antihypertensive drug therapy regimen used in both groups. Results of these studies and

new insights on the anatomy of renal arteries were taken into account in the protocols of the 2.0 generation trials (SPYRAL HTN-ON MED, SPYRAL HTN-OFF MED, and RADIANCE-HTN SOLO), in which patients were randomised to renal denervation or sham procedures. For the SPYRAL HTN--OFF study, patients were recruited with office SBP 150 mm Hg or more but not above 180 mm Hg and DBP 90 mm Hg or more (confirmed by ABPM) who did not receive antihypertensive medications or in whom drugs could be completely discontinued. At 3 months of follow-up, a difference in BP lowering by ABPM was found between the groups in favour of the renal denervation group (24-hour mean SBP –5.0 mm Hg, 24-hour mean DBP –4.4 mm Hg). The same baseline BP values were the entry criteria in the SPYRAL HTN-ON MED study but patients received 1–3 antihypertensive drugs for at least 6 weeks. At 6 months of follow-up, denervation of main renal arteries and their branches resulted in more pronounced SBP and DBP lowering compared to the sham procedure (mean between-group differences by ABPM: 24-hour mean SBP –7.4 mm Hg, 24-hour mean DBP –4.1 mm Hg). Procedure-related adverse effects were not observed in either study. Of note, the proportion of patients compliant with drug therapy did not exceed 60%, as evaluated by laboratory tests for the presence of recommended medications.

In contrast to use of the four-electrode Symplicity catheter which allows radiofrequency current ablation, renal denervation in the RADIANCE-HTN SOLO study involved ultrasound ablation of the renal arterial system. The study included hypertensive patients with BP below 170/105 mm Hg off drugs, in whom up to 1–2 antihypertensive medications were previously used and discontinued 4 weeks earlier. At 2 months of follow-up, daily SBP lowering by ABPM was –8.5 mm Hg in the denervation group compared to –2.2 mm Hg in the control group. During further follow-up, between 2 and 5 months after the procedure, patients with BP persistently above 135/85 mm Hg in home measurements received amlodipine, followed by addition of an ACEI or ARB, and ultimately hydrochlorothiazide if required. At 6 months of follow-up, the proportion of patients requiring drug therapy was lower in the denervation group (65.2%) compared to the control group (84.5%).

In the denervation group, daily SBP lowering was more pronounced compared to the sham procedure group (–18.1 ± 12.2 *vs.* –15.6±.13.2 mm Hg, P = 0.024). Results of the SPYRAL and RADIANCE-HTN trials were not available at the time the 2018 ESC/ESH guidelines were prepared, and thus renal denervation received a class III recommendation in the European guidelines (not recommended as a routine procedure in the management of hypertension). Results of pilot studies indicate a beneficial effect of renal denervation on the improvement of the glycaemic profile, the apnoea-hypopnea index (AHI) in patients with obstructive sleep apnoea, and renal function in patients with chronic kidney disease. Currently, pending confirmation of the long-term effectiveness of renal denervation, it is recommended that patient selection for this procedure should be limited to specialised hypertension units, and these procedures should be performed by experienced invasive cardiologists.

5.17. Life-threatening conditions

Conditions that require a rapid intervention due to high BP values (≥ 180 and/or 120 mm Hg) may be categorised into hypertensive emergencies and urgencies.

5.17.1. Hypertensive emergencies

In hypertensive emergencies, severe BP elevation is associated with acute complications that are immediately life-threatening. Typical presentations include:

1. **Malignant hypertension** — usually grade 3 hypertension with advanced retinopathy (haemorrhages and/or papilloedema on fundoscopy), microangiopathy and disseminated intravascular coagulation, and in some cases also with encephalopathy, acute heart failure, and acute kidney injury. The hallmark of this condition is fibrinoid necrosis within small arteries and arterioles in the kidneys, retina, and brain. The term "malignant" suggests very poor outcomes without adequate treatment.
2. **Severe hypertension associated with other life-threatening conditions** (myocardial infarction, acute coronary syndrome, pulmonary oedema, stroke, head trauma, aortic dissection).
3. **Sudden severe BP elevation in patients with phaeochromocytoma.**
4. **Severe hypertension or preeclampsia in pregnant patients.**

Symptoms and signs of hypertensive emergencies depend on the affected organs but common manifestations include headache, vision disturbances, chest pain, dyspnoea, dizziness, and neurological deficits. In patients with hypertensive encephalopathy, excessive sleepiness, lethargy, tonic seizures, and cortical blindness may precede loss of consciousness. Focal neurological signs are rare and should always raise a suspicion of stroke. Diagnostic tests recommended in patients with suspected

Table XXXI. Diagnostic tests recommended in patients with suspected hypertensive emergencies

Basic tests regardless of a potential cause
Haemoglobin, platelet count, fibrinogen Electrolytes Creatinine, eGFR Urinalysis (including sediment assessment for erythrocytes, leukocytes, and casts) Albumin/creatinine ratio 12-lead ECG Fundoscopy Pregnancy test in women of reproductive age
Specific tests depending on indications
Troponin, NT-proBNP Chest roentgenogram Echocardiography (aortic dissection, heart failure, cardiac ischaemia) Angio-CT of the chest and/or abdomen (suspected acute aortic syndrome) Brain CT or MRI (CNS symptoms) Renal ultrasound (renal dysfunction or suspicion or renal artery stenosis) Urine toxicology (suspicion of metaamphetamine or cocaine use)

Angio-CT — angiocomputed tomography; CNS — central nervous system; CT — computed tomography; eGFR — estimated glomerular filtration rate; MRI — magnetic resonance imaging; NT-proBNP — N-terminal pro B-type natriuretic peptide

Table XXXII. Intravenous antihypertensive medications available in Poland

Urapidil
Ebrantil 25 — 5 mg/mL (25 mg/5 mL) — 5 mL ampoules Dosing: bolus 12.5–25 mg *iv*, followed by *iv* infusion 5–40 mg/min
Nitroglycerin
Perlinganit — solution for *iv* infusion 1 mg/mL (10 mg/10 mL) — 10 mL ampoules Nitracor — solution for *iv* infusion 2 mg/mL (10 mg/5 mL) — 5 mL ampoules Dosing: 5 mg *iv*, followed by *iv* infusion 4 mg/h
Esmolol
Esmocard — 100 mg/10 mL — 10 mg/mL (100 mg/10 mL) — 10 mL ampoules Esmocard — 2500 mg/10 mL — 250 mg/mL (2.5 g/10 mL) — 10 mL ampoules Dosing: 0.5–1 mg/kg *iv*, followed by 50–300 mg/kg/min *iv*
Furosemide
Furosemide Kabi, Furosemidum Polfarmex, Furosemidum Polpharma — 10 mg/mL (20 mg/2 mL) — 2 ml ampoules Dosing: 20–40 mg *iv* initially, followed by 20 mg *iv* every 2 hours as needed; larger doses should be given as *iv* infusion In emergencies, labetalol, nicardipine, and sodium nitroprusside may also be given *iv* but these drugs are currently not available in Poland

iv — intravenous

hypertensive emergencies are listed in Table XXXI. In these circumstances, admission to an intensive care unit is required and parenteral antihypertensive therapy is often necessary. The management of hypertensive emergencies depends on the type of target organ damage, ranging from only very cautious BP reduction in acute stroke to immediate BP reduction in acute pulmonary oedema or aortic dissection. In most cases, immediate BP reduction is suggested, with the target of BP lowering by 25% within first hours of treatment using available parenteral antihypertensive medications (Tab. XXXII). Except for urgent BP lowering in stroke, there are no randomised trials that would evaluate various management strategies in patients with hypertensive emergencies. The most important factors to consider when planning the management strategy include:

— evaluation of the presence of target organ damage (and whether they require specific management in addition to BP lowering);
— recommended timing and degree of BP lowering;
— required mode of BP lowering — regarding medications, the ideal drug in hypertensive emergencies is administered intravenously, has a short half-life, and allows cautious BP reduction under strict physician supervision with continuous monitoring of the haemodynamic status;

Table XXXIII. Recommended drug therapy in specific emergencies

Clinical presentation	Timing of BP lowering and therapeutic target	First choice drugs	Alternative drugs
Malignant hypertension with or without acute kidney injury	Reduce MAP by 20–25% within several hours	Labetalol, nicardipine	Sodium nitroprusside, urapidil
Hypertensive encephalopathy	Reduce MAP immediately by 20–25%	Labetalol, nicardipine	Sodium nitroprusside
Acute coronary event	Reduce SBP immediately to < 140 mm Hg	Nitroglycerin, labetalol	Urapidil
Pulmonary oedema	Reduce SBP immediately to < 140 mm Hg	Sodium nitroprusside or nitroglycerin (with loop diuretic)	Urapidil (with loop diuretic)
Acute aortic dissection	Immediately reduce SBP to < 120 mm Hg and heart rate to < 60 bpm	Esmolol and sodium nitroprusside or nitroglycerin or nicardipine	Labetalol or metoprolol
Eclampsia or severe preeclampsia, HELLP	Immediately reduce SBP to < 160 mm Hg and DBP to < 105 mm Hg	Labetalol or nicardipine and magnesium sulphate	Consider delivery

BP — blood pressure; bpm — beats per minute; DBP — diastolic blood pressure; HELLP — haemolysis, elevated liver enzymes, low platelets; MAP — mean arterial pressure; SBP — systolic blood pressure

— rapid uncontrolled BP lowering is not recommended due to the risk of complications. The recommended drug therapy in specific emergencies is shown in Table XXXIII.

5.17.2. Hypertensive urgencies

In hypertensive urgencies, largely elevated BP is not associated with an immediately life-threatening condition. Most patients do not require hospital admission, but immediate combined oral antihypertensive therapy is needed, and less frequently parenteral therapy should be initiated. Hypertensive urgencies include conditions associated with antihypertensive drug withdrawal or dose reduction, epistaxis, acute glomerulonephritis with high BP values, drug-induced hypertension, and hypertension associated with spinal cord trauma.

6. Non-blood pressure-lowering therapy (treatment of concomitant risk factors) in patients with hypertension

6.1. Lipid-lowering drugs

Hypercholesterolemia is more prevalent in hypertensive patients compared to the general population, as is atherogenic dyslipidaemia in patients with concomitant diabetes. Multiple clinical trials on the use of statins in primary and secondary prevention, in which hypertensive patients constituted a significant proportion of the study populations, indicate that an optimal reduction of the global cardiovascular risk may be obtained by simultaneous reduction of BP and LDL cholesterol level. This particularly justifies use of so-called hybrid SPC, containing both a BP-lowering agent and a lipid-lowering agent in one tablet. In this context, combinations of two antihypertensive agents recommended for treatment initiation (e.g., a RAAS inhibitor and a calcium antagonist or a thiazide-type diuretic) with a statin seem particularly valuable.

In 2019, new European guidelines may be expected that will recommend lower target LDL cholesterol levels in patients at risk of cardiovascular events, including patients with hypertension. Before the ESC guidelines will be made available to the public, the Polish Cardiac Society Section on Cardiovascular Pharmacotherapy in 2018 has published their Polish recommendations with much lowered target LDL cholesterol levels in many patient groups. In the present PTNT guidelines, these target values are recommended in patients with hypertension depending on the level of their cardiovascular risk (Tab. XXXIV–XXXVI).

6.2. Antiplatelet therapy

In patients with hypertension and cardiovascular disease, use of acetylsalicylic acid (ASA) is mandatory based on the general guidelines of cardiac societies that recommend a 75 mg dose. Use of ASA should not be limited by the degree of BP control but is a factor that makes good BP control particularly necessary.

A recently published large metaanalysis that evaluated the rates of major bleeding events in patients receiving long-term ASA treatment has changed the approach to the use of this drug in primary prevention. It has been shown that the net benefits of ASA, measured as the difference between the car-

Table XXXIV. Non-blood pressure lowering treatment strategies in patients with hypertension

Assessment of the global cardiovascular risk using the Framingham risk score and the SCORE risk estimation chart (recalibrated nationally as the Pol-SCORE risk chart) is recommended in patients with hypertension to determine indications for non-blood pressure lowering treatment
In patients at low cardiovascular risk (no additional risk factors, Pol-SCORE risk < 1%), statin treatment should be considered if LDL cholesterol level is > 115 mg/dL
In patients at moderate cardiovascular risk (additional risk factors, Pol-SCORE risk 1–5%), statin treatment, in some cases combined with ezetimibe, should be considered to lower LDL cholesterol level to < 100 mg/dL
In patients at high cardiovascular risk (multiple risk factors and/or target organ damage and/or diabetes or Pol-SCORE risk 5–20%), statin treatment, in some cases combined with ezetimibe, is recommended to lower LDL cholesterol level to < 70 mg/dL
In patients at very high cardiovascular risk (established cardiovascular disease, including an acute coronary or cerebrovascular event despite LDL cholesterol level < 70 mg/dl or Pol-SCORE risk > 20%), maximum tolerated statin dose combined with ezetimibe is recommended to lower LDL cholesterol level to < 55 mg/dL
In patients at extremely high cardiovascular risk (multiple cardiovascular events despite LDL cholesterol level < 55 mg/dl), it is recommended to add PCSK9 inhibitor therapy to the maximum tolerated statin dose combined with ezetimibe to lower LDL cholesterol level to < 35 mg/dL
Use of allopurinol at the target dose of ≥ 300 mg/d should be considered in hypertensive patients at high cardiovascular risk with asymptomatic hyperuricaemia, and even with serum uric acid level > 5–6 mg/dL, despite normal renal function, aiming for the target level of < 5 mg/dL
Use of acetylsalicylic acid 75–150 mg/d or other recommended antiplatelet therapy is recommended for secondary cardiovascular event prevention in hypertensive patients regardless of the degree of BP control
Use of acetylsalicylic acid is not recommended for primary prevention in hypertensive patients regardless of the cardiovascular risk level

BP — blood pressure; LDL — low density lipoprotein; PCSK9 — proprotein convertase subtilisin/kexin 9; SCORE — Systematic Coronary Risk Evaluation

Table XXXV. Polish Society of Hypertension guidance on LDL cholesterol level lowering based on the Third Declaration of Sopot

Risk category	Clinical condition or presence of risk factors or 10-year Pol-SCORE risk	Target LDL cholesterol level
Low	No additional risk factors	**< 115 mg/dL** (< 3.0 mmol/L)
Moderate	< 2 risk factors and Pol-SCORE risk < 5%	**< 100 mg/dL** (< 2.6 mmol/L)
High	≥ 2 risk factors and Pol-SCORE risk 5–20% Diabetes or stage 3–4 CKD with no other risk factors	**< 70 mg/dL** (< 1.8 mmol/L)
Very high	Progression of atherosclerotic cardiovascular disease in patients in whom LDL cholesterol level < 70 mg/dL was achieved and maintained Acute coronary syndrome, coronary artery disease, carotid artery disease or peripheral arterial disease Previous revascularization Pol-SCORE risk > 20% Diabetes or stage 3–4 CKD with 1 or more other risk factors Familial hypercholesterolaemia Family history of premature atherosclerotic cardiovascular disease (< 55 years in men, < 65 years in women) Established cardiovascular disease in patients with diabetes, stage 3–4 CKD or familial hypercholesterolaemia	**< 55 mg/dL** (< 1.4 mmol/L)
Extremely high	Multiple previous cardiovascular events and/or revascularizations Percutaneous revascularization at specific anatomical locations (e.g., patients after percutaneous revascularization for left main coronary artery disease and/or with multivessel coronary artery disease) Generalized atherosclerosis — involvement of multiple vascular beds with additional risk factors Progression of atherosclerotic cardiovascular disease in patients in whom LDL cholesterol level < 55 mg/dL was achieved and maintained	**< 35 mg/dL** (< 0.9 mmol/L)

CKD — chronic kidney disease; LDL — low density lipoprotein; SCORE — Systematic Coronary Risk Evaluation

Table XXXVI. Polish Society of Hypertension guidance on the use of lipid-lowering drugs based on the Third Declaration of Sopot

Risk category	Use of lipid-lowering drugs	Target LDL cholesterol level
Low	Low-dose statin	**< 115 mg/dL** (< 3.0 mmol/L)
Moderate	Moderate-dose statin	**< 100 mg/dL** (< 2.6 mmol/L)
High	Moderate- to high-dose statin Ezetimibe	**< 70 mg/dL** (< 1.8 mmol/L)
Very high	High-dose statin Ezetimibe	**< 55 mg/dL** (< 1.4 mmol/L)
Extremely high	High-dose statin Ezetimibe PCSK9 inhibitor	**< 35 mg/dL** (< 0.9 mmol/L)

LDL — low density lipoprotein; PCSK9 — proprotein convertase subtilisin/kexin 9; SCORE — Systematic Coronary Risk Evaluation

diovascular event rate reduction and the increase in the major bleeding event rate, have not been clearly established in this patient population. Until now, use of ASA for this indication required evaluation of the risk-to-benefit ratio. In the current 2018 ESC/ESH guidelines, use of ASA for primary prevention of cardiovascular events is not recommended. In view of this abandonment of ASA for primary prevention in hypertensive patients at high cardiovascular risk, use of alternative substances with antiaggregant properties that have been evaluated in clinical trials (e.g., standardised tomato extract which exerts a weaker antiplatelet effect compared to ASA but has a more pleiotropic activity range) may be considered.

6.3. Uric acid-lowering therapy

In the 2018 ESC/ESH guidelines, elevated uric acid level has been considered a novel significant cardiovascular risk factor in patients with hypertension. A similar position has been taken in the present document. Uric acid production in the setting of ischaemia is associated with free radical formation and endothelial dysfunction. It has been shown that use of xanthine oxidase inhibitor allopurinol leads to improved endothelial function and aortic compliance, and the result of more recent studies indicate a reduction of the cardiovascular event risk, particularly with allopurinol dose of 300 mg/d. For this reason, following the international expert consensus statement, the present PTNT guidelines recommend consideration of allopurinol use in hypertensive patients at high cardiovascular risk if uric acid level is elevated (> 5–6 mg/dL) despite normal renal function.

7. Methods to improve blood pressure control in hypertensive patients

Published studies indicate that many hypertensives are unaware of their elevated BP values, and even if they are aware of their hypertension, many individuals remain untreated. In addition, target BP levels are infrequently reached regardless of whether the treatment is undertaken by specialists or general practitioners. At the same time, the proportion of patients aware of their hypertension and the need to control elevated BP increases slowly and this trend is seen only in some patients, mostly in the secondary prevention population. It is currently believed that providing patients with easily comprehensible educational materials distributed by media or available in physician offices and pharmacies has a beneficial effect of patient knowledge and motivation.

In clinical practice, two major causes of poor BP control may be identified:

1. Poor patient compliance.
2. Therapeutic inertia.

Non-compliant patients may be divided into those who permanently discontinue the therapy and those who use their medications in an inappropriate way (e.g., irregular drug intake, including delayed dosing and multiple short-lasting treatment interruptions). Poor patient compliance is also a very frequent problem in regard to the recommended lifestyle changes. Regarding use of prescribed medications, studies indicate that more than one third of patients discontinue antihypertensive drug therapy by 6 months, and about half of patients discontinue it by one year. In addition, about 10% of patient forget to take their

medication on any given day. For this reason, efforts to increase patients' compliance and persistence are a duty of the treating physician. Studies indicate that the elderly patients are more motivated to treatment. However, they are characterised by greater persistence but lower compliance compared to younger subjects. Some of the causes of low patient-physician cooperation worsen in the elderly age, including memory problems, difficulties with understanding the dosing regimen, worse tolerance of normal BP values, financial problems with prescription filling, concomitant disease giving rise to more troubling complaints, and the need to take multiple medications. Patients, particularly the elderly, require time to be taken to explain the dosing regimen and the importance of antihypertensive treatment, and sometimes engage the family members or enquire about the financial situation of the patients. Two of the changes in the management of hypertension highlighted in the present guidelines may improve compliance. Somewhat higher target BP values in the elderly may improve treatment tolerance and mitigate the effect of treatment on quality of life in this patient group. The role of SPC in the antihypertensive therapy has increased, and with a decreased number of tables and simplified dosing regimens, it may be possible to both increase compliance and decrease therapeutic inertia, or no treatment intensification by the physician despite inadequate BP control in the patient. Increased use of SPC may be facilitated by wide reimbursement of this treatment for indications discussed in the present guidelines.