Guidelines for the management of hypertension in Poland 2024 — the position paper of the Polish Society of Hypertension and Polish Cardiac Society experts

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LIST OF ABBREVIATIONS

ABI	ankle-brachial index
ABPM	ambulatory blood pressure monitoring
ACEI	angiotensin-converting enzyme inhibitor
ACR	albumin-creatinine ratio
AF	atrial fibrillation
ARB	angiotensin II receptor AT1 blocker
ARNI	angiotensin receptor-neprilysin inhibitor
ASA	acetylsalicylic acid
BARKH	brain, arteries, retina, kidneys, heart
BB	beta-blocker
BMI	body mass index
BP	blood pressure
CAC	calcium score
CCB	calcium channel blocker
CKD	chronic kidney disease
COVID-19	coronavirus disease 2019
COX-2	cyclooxygenase 2
CPAP	continuous positive airway pressure
CT	computed tomography
CV	cardiovascular
DBP	diastolic blood pressure
ECG	electrocardiogram
eGFR	estimated glomerular filtration rate
ESC	European Society of Cardiology
ESH	European Society of Hypertension
FMD	fibromuscular dysplasia
GLP-1	glucagon-like peptide 1
HbA1c	glycated hemoglobin
HELLP	hemolysis, elevated liver enzymes, low platelets
HF	heart failure
HFpEF	heart failure with preserved ejection fraction
HFrEF	heart failure with reduced ejection fraction
HMOD	hypertension-mediated organ damage
HR	heart rate
HRT	hormone replacement therapy
HT	hypertension
ISH	isolated systolic hypertension
KCCQ-CCS	Kansas City Cardiomyopathy Questionnaire — The Clinical Summary Score
LEAD	lower extremity arterial disease
LVH	left ventricular hypertrophy
MAP	mean arterial hypertension
MMM	May Measurement Month
MRA	mineralocorticoid receptor antagonist
MS	metabolic syndrome
NSAID	non-steroidal anti-inflammatory drug
NT-proBNP	N-terminal pro-B-type natriuretic peptide
op-BP	opportunistic blood pressure measurements
OC	oral contraceptive
OGTT	oral glucose tolerance test
OSA	obstructive sleep apnea
PA	primary hyperaldosteronism
PAD	peripheral arterial disease
PCOS	polycystic ovary syndrome
PCSK9	proprotein convertase subtilisin/kexin 9
PE	pre-eclampsia
PRES	posterior reversible encephalopathy syndrome
PTD	Polish Diabetes Association
PTK	Polish Cardiac Society
PTNT	Polish Society of Hypertension
PUFA	polyunsaturated fatty acid
PWV	brachial-ankle PWV
RRI	renal resistive index
SBP	systolic blood pressure
SCD	sudden cardiac death
SPC	single-pill combination
TIA	transient ischemic attack
TLD/TD	thiazide-like diuretic/thiazide diuretic
TSH	thyrotropin-stimulating hormone
UACR	urine albumin-creatinine ratio
USG	ultrasonography
X-ray	radiological examination

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1. INTRODUCTION

For years, hypertension (HT) has remained one of the most common risk factors leading to cardiovascular disease (CVD) and death both in Poland and worldwide [1–5]. Therefore, its effective treatment has become a priority for hypertensiologists, cardiologists, general practitioners (GPs) and physicians from other specialities. In the past, the ESH and ESC cooperated on publishing the joint version of the HT treatment guidelines; however, the two societies created the most recent publications separately [3–5, 7, 8]. To increase the effectiveness of HT therapy, the activities of all specialists should be coordinated and based on common guidelines. Therefore, the Board of the Polish Society of Hypertension (PTNT) and the Board of the Polish Cardiac Society (PTK) agreed to develop a joint document Guidelines for the management of hypertension in Poland 2024 — the position of PTNT/PTK Experts. The text was first assessed by reviewers and then submitted to the Committee of 30 Polish HT Experts for opinion. Each controversial statement had to be supported by at least 23 of the 30 Committee members to be included in the final document.

Based on the analysis of the National Health Fund (NFZ) data from 2018–2022, the number of HT patients in Poland remains stable and it is approximately 11 million people (Figure 1.1). The disease affects 34%–35% of adults [9]. Additionally, global data show that HT affects a total of approximately 5% of the population aged 0–18 [10]. The disease is rarely diagnosed in the first years of life, but during puberty, the incidence of HT increases significantly, especially in boys. Polish data indicate that in adolescents aged 18 years, HT affects 9% of the population and it is almost 16% in boys, which corresponds to the prevalence of HT in young adults [11].

The 2019–2021 analysis, excluding patients with heart failure (HF), found that 9.5–10.3 million people are taking antihypertensive medication [12]. In Poland, the incidence of HT is among the highest in Europe, in both women and men [13]. Monotherapy still remains the most common treatment (54% of patients in 2021). Beta-blockers (BBs) remain the most commonly used group of drugs. The popularity of single-pill combinations (SPCs) increased in the period from 2019 to 2021. In 2021, 30% of patients taking antihypertensive drugs used SPCs combining two drugs and 3% used SPCs combining three drugs. Among patients undergoing combination treatment (2 drugs or more), 46% used SPCs combining two drugs. Among patients treated with three or more antihypertensive drugs, the share of patients using SPCs combining three drugs was 20%. There is no current data on the effectiveness of HT treatment in Poland. The 2013–2014 WOBASZ study showed that effective HT therapy was achieved in 23% of the participants [14]. In contrast, the 2018–2019 POLSENIOR2 study revealed that HT affected three out of four people aged 60 and older. HT control was achieved in one-third of the population — 33%, including 39% receiving antihypertensive medication [15]. A slightly higher share of patients aged 65 and older who achieved blood pressure (BP) control was confirmed in the 2017–2018 NOMED-AF study [16]. In 2021, during the May Measurement Month (MMM) campaign, BP was measured/assesed in 1699 persons. The control was achieved by 31% of HT patients, including 60% undergoing treatment [17]. The BP control may have been negatively affected by the coronavirus disease 2019 (COVID-19) [18–21].

In this document, the level of recommendation is not provided. Instead, the assessed recommendations and degrees of recommendation were taken from the ESH and ESC guidelines and presented in the figures. The purpose of this approach is to make it easier to understand what should definitely be done and what is worth considering. The graphical representation of the recommendations seems more useful in practice.

2. BP MEASUREMENTS

BP measurements (Figure 2.1) should be taken using validated devices. This means that their accuracy was assessed in a clinical trial in accordance with accepted protocols and the results were published in a peer-reviewed scientific journal. A list of such devices can be found at: www.dobrzemierze.pl and www.stridebp.org [3, 5].

BP measurements at the doctor's office are considered crucial in diagnosing and evaluating the effectiveness of HT treatment [4, 5]. However, studies indicate that out-of-office measurements have greater prognostic value [23, 24]. More than 90% of HT patients in Poland take home BP measurements [22], which, together with access to ambulatory blood pressure measurements (ABPM) through the National Cardiac Network and Coordinated Care, allows to consider out-of-office methods as the main means of BP monitoring [25]. Office BP measurements play an additional and verifying role.

2.1. BP classification

The correlation between BP values and cardiovascular risk in persons without blood lowering therapy is linear, starting from values as low as 100–110 mm Hg for systolic BP [26–28]. For this reason, describing BP values as "normal" may be misleading in terms of their association with cardiovascular risk. In the presented document, three BP categories (systolic and diastolic BP values for office measurements) are introduced:

- **optimal BP**: below 120 and below 70 mm Hg;
- **elevated BP**: 120 to 139 and/or 70 to 89 mm Hg;
- **HT**: 140 and/or 90 mm Hg or greater.

The purpose of the new BP classification is not only to simplify BP categories used so far, but also to promote preventive measures against HT development and to reduce CV disease risk in people with elevated BP. In the ESC guidelines, the lowest BP category is referred to as "non-elevated" BP [5]. This may imply that BP values in this category are incorrect; moreover, such a term is not motivating to

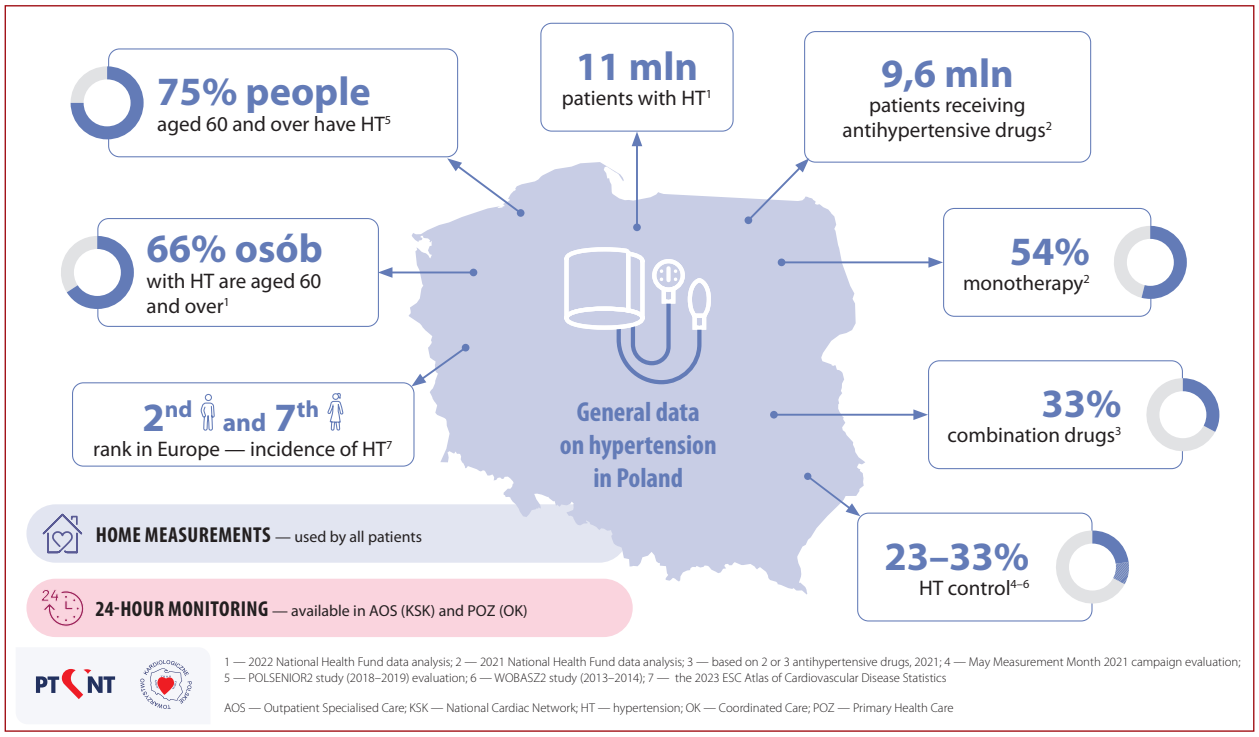


Figure 1.1. The prevelance of hypertension (HT) in Poland. Developed based on [9, 12, 14, 15, 17, 22]

pursue healthy lifestyle. Therefore, it is proposed to refer to the BP values below 120 and below 70 mm Hg as "optimal".

Detailed cut-off values for each category for the different BP measurement methods are presented in Figure 2.2. As the white coat effect becomes gradually less evident along with lower BP values, the criteria for "optimal BP" are the same for office and out-of-office BP [5]. Table 2.1 shows the present and new classification of BP categories.

2.2. Office BP

BP measurements taken in healthcare facilities or by medical staff are referred to as office BP. For decades, office BP constituted basic method of BP assessment. However, the wide availability of out-of-office BP measurement methods that better illustrate CV disease risk is gradually reducing role of office BP. Office measurements can be performed with an aneroid sphygmomanometer or using a validated automatic device. The cuff should be adjusted according to arm circumference and at least two, preferably three, measurements should be taken on the same arm, one minute apart. The result is presented as the average of the last two measurements [2, 4, 5, 29].

Unattended automatic office BP measurements, due to the lack of clearly defined BP thresholds for this method and the fact that they do not increase the accuracy of the cardiovascular risk assessment compared to office measurements, are not currently recommended [30, 31].

2.3. Home BP

Home BP measurements are self-measurements taken by the patient or another person. In Poland, almost all patients with HT have an access to personal BP measurement devices. Home BP monitoring over several consecutive days provides more comprehensive insight into HT control than a single 24-hour recording. Reliable home measurements help to identify patients with elevated BP. Additionally, self BP monitoring engage patients which translates to better adherence to therapy. Automatic validated devices with an appropriately selected arm cuff are recommended. Validated wrist BP measuring devices are also available, including those for overnight measurements [2, 4, 5, 29]. Interpretation of the results is shown in Figures 2.2 and 2.3.

What is the optimal regimen for home BP measurements?

- HT diagnosis, treatment control and pre-visit recommendations: BP measurements on 7 consecutive days (not less than 3 days) should be taken following the 2 × 2 scheme, i.e. two measurements in the morning and two in the evening , before meals and medications. The measurements should be tak en one after the other on the same arm.
- Outside the 7-day period: the frequency of measurements is determined individually, usually several times a week or month, at different times. Two measurements should always be taken, one after the other, and both results should be recorded.

2.4. Ambulatory blood pressure monitoring

Ambulatory blood pressure monitoring (ABPM) is a method of monitoring the BP 24 hours a day using a device worn by

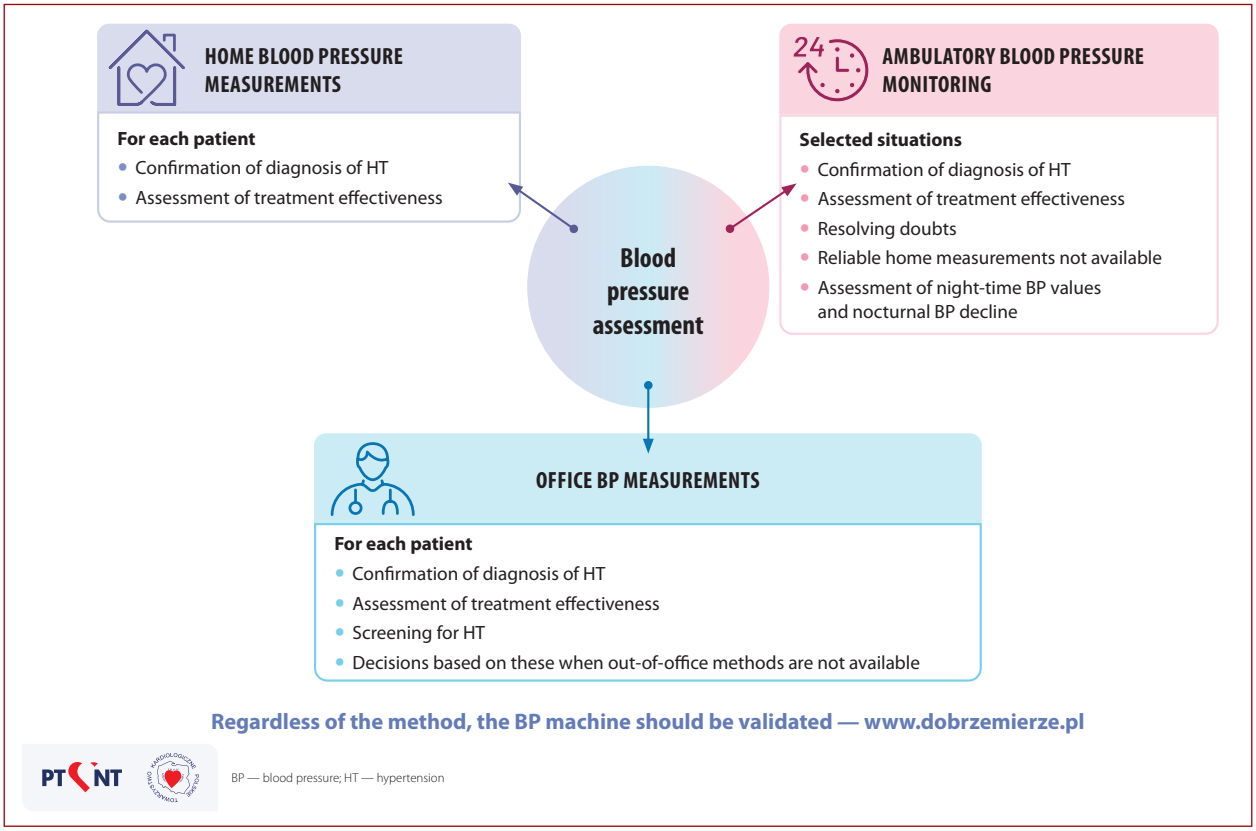


Figure 2.1. Selection of blood pressure (BP) measurement method

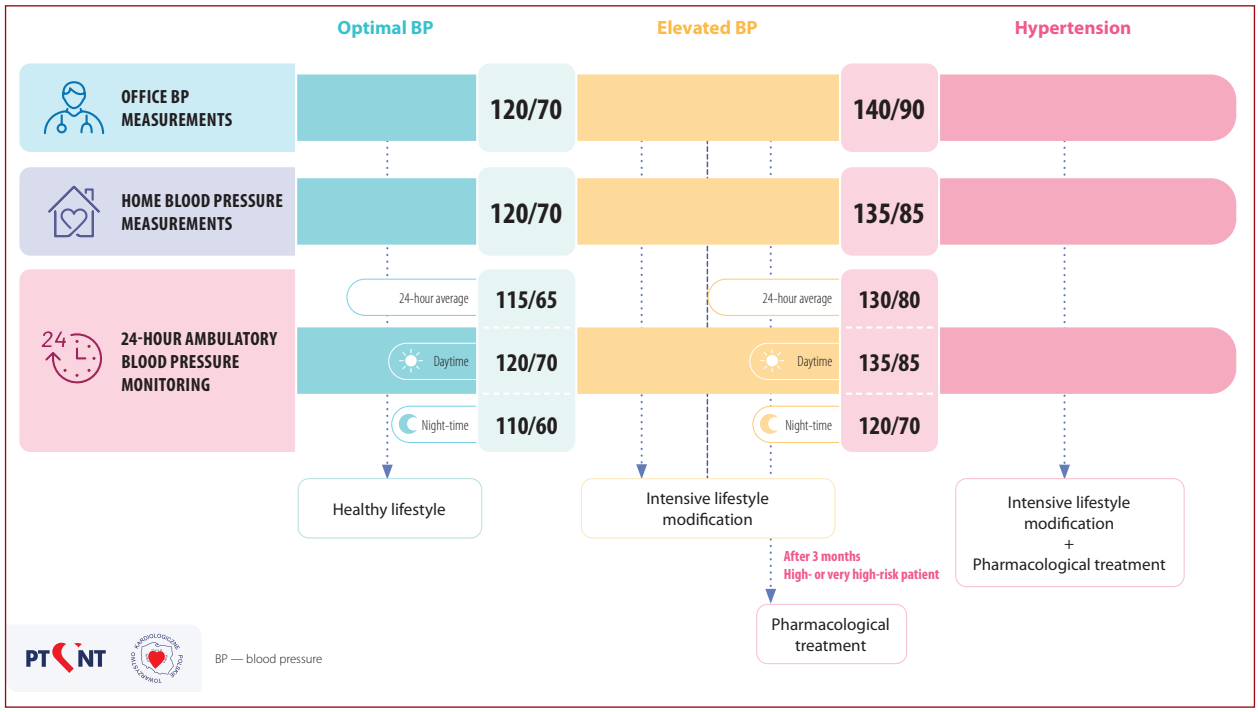


Figure 2.2. Blood pressure (BP) cut-off values and initiation of hypertension (HT) treatment. Based on [2, 4, 5, 29]

Table 2.1. Present and new classification of blood pressure (BP) categories. Based on [4, 5]

Systolic and diastolic BP values [mm Hg]		Present BP categories	New BP categories
< 120 and < 120 and/or	< 70	Optimal BP	Optimal BP
	70–79		Elevated BP
120–129 and/or 80–84		Normal BP	
130–139 and/or 85–89		Normal high BP	
≥ 140 and/or ≥ 90		HT grade 1.	HT
≥ 160 and/or ≥ 100		HT grade 2.	
≥ 180 and/or ≥ 110		HT grade 3.	

Where BP values fall into different categories, the higher category should be considered

Abbreviations: HT, hypertension

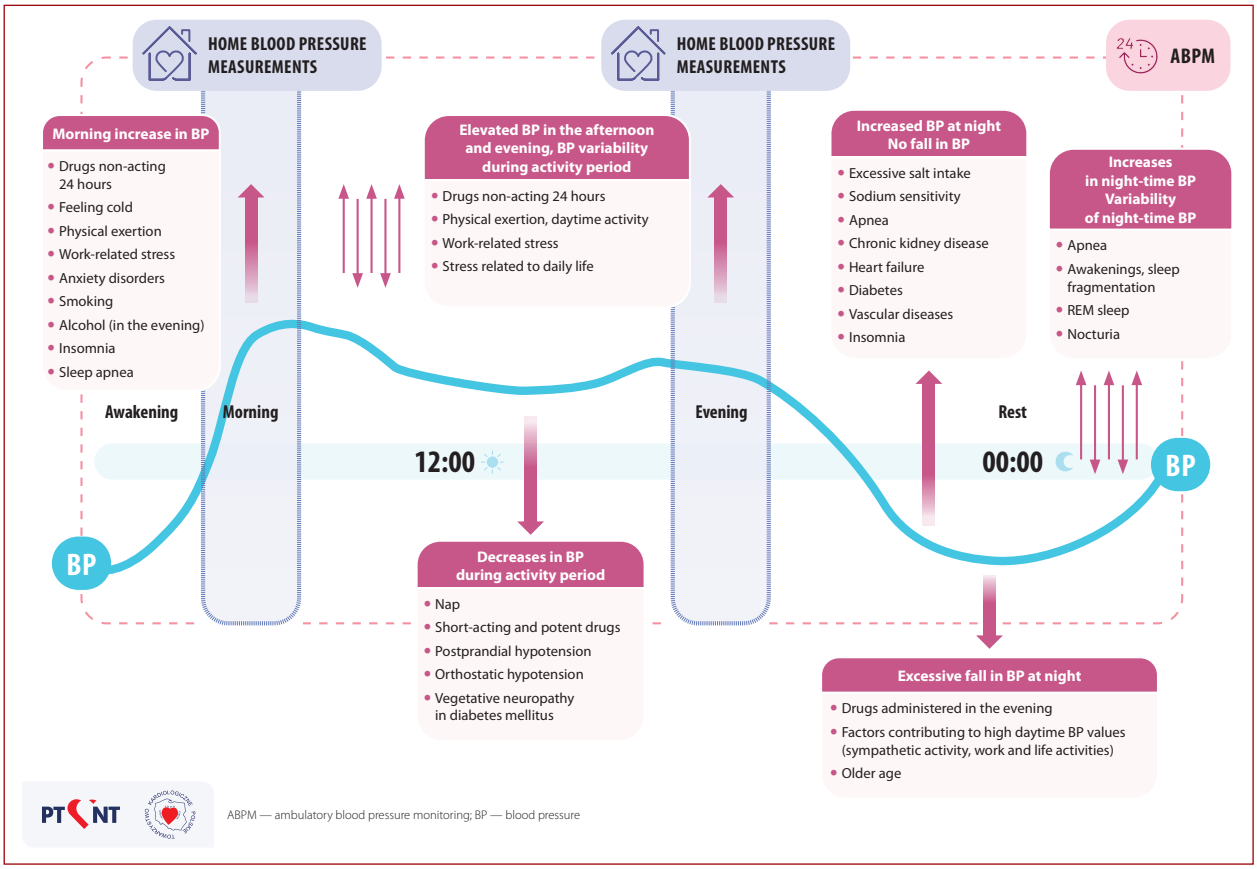


Figure 2.3. Interpretation of blood pressure (BP) values and profile in out-of-office measurements. Based on [35–40]

the patient under everyday conditions. It is a key method for verifying BP values obtained during office and out-of-office BP measurements (Figure 2.1). It also allows the verification of BP values at night. Validated devices with an appropriately sized cuff should be used for that purpose. The measurements should be taken every 15–20 minutes during the day and every 30 minutes at night. Day and night are determined after registration is completed based on the rest time reported by the patient. For the registration to be considered valid, at least 70% of the measurements must provide reliable results. The results are interpreter according to Figures 2.2 and 2.3.

2.5. Situational hypotension

Conditions which may evoke hypotension and further confer CV events and premature death risks include the following:

- orthostatic hypotension;
- postprandial hypotension;
- post-exercise hypotension;
- sleeptime hypotension.

Confirmation of situational hypotension as listed above usually require individualized antihypertensive therapy.

As part of the initial assessment of patients, it is recommended to perform an orthostatic test by measuring BP

1 and 3 minutes after changing the position from sitting/lying to standing (the patient should stay in a sitting/lying position for ≥5 minutes). Orthostatic hypotension is diagnosed when there is a decrease in systolic BP of ≥20 mm Hg or diastolic BP of ≥10 mm Hg. It is recommended to repeat the orthostatic test when suggestive symptoms of orthostatic hypotension occur [5].

2.6. Opportunistic BP measurements and BP measurements in pharmacies

BP measurements that do not meet the criteria of the categories described above are referred to as opportunistic (op-BP) measurements. Examples of op-BP are BP measurements carried out during health awareness events (e.g. White Saturdays, the international MMM campaign, the World Heart Day, etc.) [17]. The non-standard course of the op-BP measurements makes the BP readings difficult to clearly interpret, but this type of activities engage participants in preventive actions. It is recommended that the op-BP measurement organisers consider the following:

- printing/saving the op-BP measurement result;
- name of the device used and the size of the cuff;
- recommending the person to consult the result with the physician during the next visit (or, in the case of an abnormal result, a recommendation to contact the physician urgently — in the case of BP >180/110 mm Hg).

Systematic incorporation of op-BP into non-medical services, such as hairdressing services, have additional potential. Regular visits to barbershops during which clients measure their BP and receive feedback on HT have been shown to increase the effectiveness of blood-lowering treatment, especially in high CV risk populations [32].

A special category of op-BP measurements are those performed in pharmacies; the procedure which was not regulated in Poland until 2023. Currently, pharmacists are authorized to measure BP according to the office measurement standard. The aim of that service, together with drug review as part of the pharmaceutical care is to improve therapeutic safety and adherence to blood lowering therapy [33, 34].

2.7. Night-time BP

Lack of BP fall during sleep, or the so-called non-dipping, is a condition in which BP does not fall at night by a physiological 10%–20% compared to daytime values. Such a condition, as well as elevated BP at night, excessive night-time fall or morning surge, is associated with a higher risk of cardiovascular diseases such as HT, HF, stroke or myocardial infarction. The most favourable BP profile that is associated with the lowest CV events risk is characterized by a moderate reduction in BP during sleep and no excessive surge in the morning [35–40].

How to assess BP values at night?

- Ensure that ABPM has been carried out correctly using a validated device.
- Ask the patient if the quality and length of sleep were adequate and if BP measurements did not interrupt their sleep.
- Check whether the rest period specified in the result matches the actual rest time.
- Assess the absolute BP values at night, the night-time fall and morning increase.
- A useful addition to the ABPM machines is the motor activity assessment function [consider the use of the available ABPM machine function as a supplement], which helps to assess the quality and quantity of the patient's sleep during the recording.

3. HT DIAGNOSIS

BP tends to rise with age. The initial BP rise is mainly driven by genetic factors, whereas the environmental factors play a pivotal role later in life. The cut-off values that define HT are set arbitrary. It is BP value beyond which its' reduction results in longer predicted life span and better quality of life. In recent years, a large body of evidence has emerged showing the benefits of lower target BP values (<130/80 mm Hg). However, the European guidelines uphold the cut-off for the diagnosis of HT at 140/90 mm Hg [4, 5].

The authors of this document confirm 140/90 mm Hg in office BP to be diagnostic for HTN (and corresponding values in out-of-office measurements; Figure 2.2). However, it is emphasized that BP in the ranges of 120–139/70–89 mm Hg, referred to as "elevated BP", require intensive lifestyle changes and, in some clinical settings, also pharmacotherapy [5].

Hypertension is diagnosed based on:

- a reliable history indicating high BP or use of antihypertensive therapy;
- BP values on home BP measurements (see section 2);
- BP values on ABPM (see section 2);
- office BP, only if confirmed by home measurements/ABPM or when office BP is ≥180/110 mm Hg after excluding reversible causes (see Figure 3.1).

Figure 2.2 presents the BP cut-off values for the diagnosis of HT depending on the method of measurement. BP defined as elevated is also associated with a higher cardiovascular risk. Figure 3.1 presents the principles for the HT diagnosis.

The white coat effect occurs when BP in office measurements is within the range of values consistent with HT, but remains within the range of elevated BP or optimal BP values during home measurements or ABPM. Patients with that condition may be at increased cardiovascular risk and should be monitored regularly, i.e. every 6–12 months. In

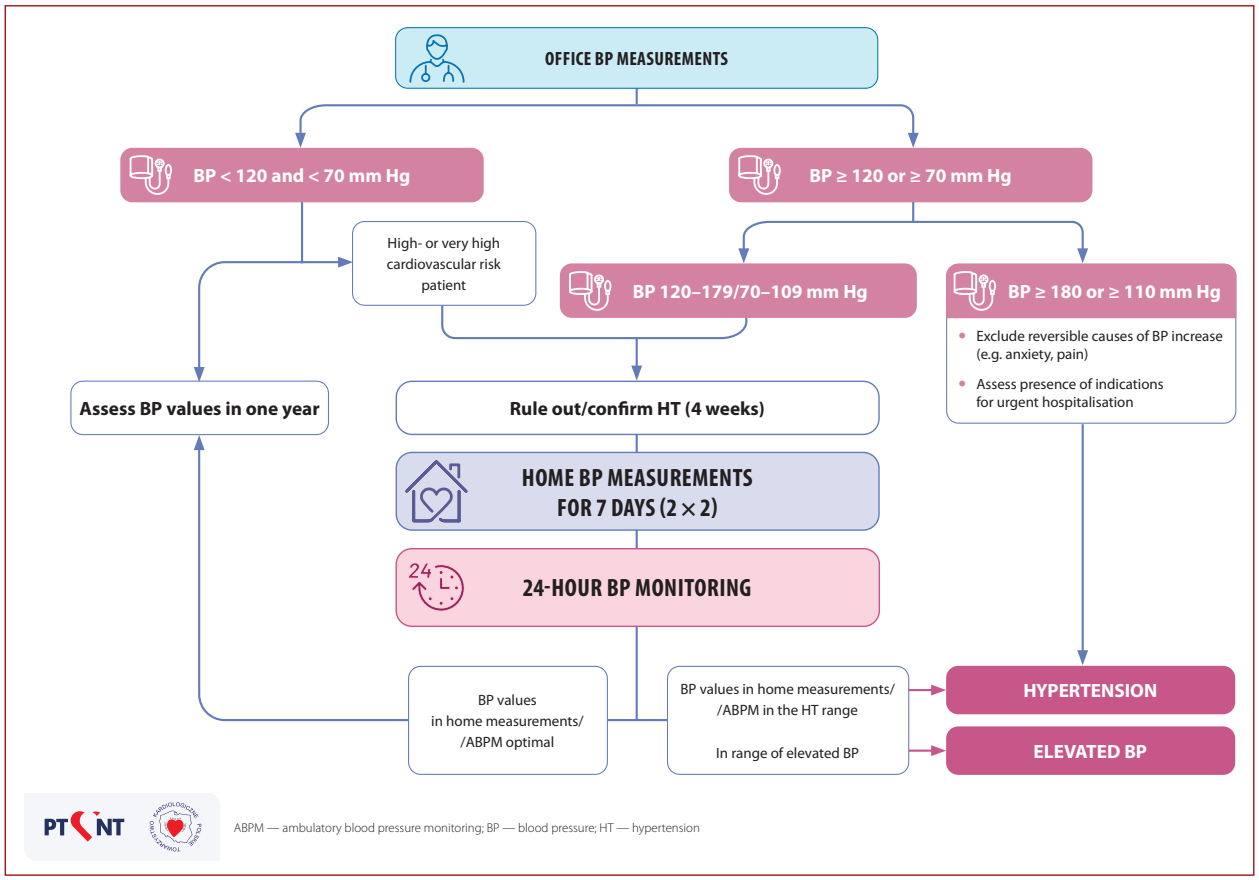


Figure 3.1. Principles of hypertension diagnosis

specific cases, especially in patients with organ complications or diagnosed CV disease, the initiation of antihypertensive treatment should be considered.

How often to assess BP values to detect HT?

Since BP increases throughout life and the rate of increase depends on many factors, BP measurement (office or at home) should be performer at least once a year in every adult.

People with elevated BP who are not on antihypertensive treatment should have their BP measured every three months. In the last case, it is also worth considering annual 7-day home measurements to get a more accurate picture of BP changes.

Masked HT is defined by office BP readings lower than 140/90 mm Hg which coincide with elevated home or 24-h ambulatory values. Such a condition should be treated as HT and requires appropriate treatment (Figure 3.1).

4. CLINICAL ASSESSMENT, DIAGNOSTIC TESTS AND ASSESSMENT OF TARGET ORGAN DAMAGE

4.1. Clinical assessment of the HT patient

Clinical assessment of a patient with HT includes patient's medical history, physical examination, as well as routine and extended tests/evaluation. The purpose is to detect the increased risk of CV diseases and to identify specific comorbidities and potential causes of secondary HT. Additionally, the aim of the assessment is to identify HT-mediated organ damage (HMOD). The key information on HT to be obtained from the anamnesis and physical examination is summarized in Tables 4.1 and 4.2.

4.2. Routine and addtional evaluation

Routine evaluation

Routine medical assessment and additional tests to be performed at the diagnosis and monitored as indicated are summarized in Figure 4.1 and Table 4.3.

Table 4.1. Key information on hypertension (HT) to be obtained during a medical interview

Patient's history of HT
• Age at which HT was diagnosed (disease duration) • Stable versus rapidly increasing BP (or increasing need for antihypertensive medication) • Record of current and past BP values obtained during home measurements • Current/previous use of antihypertensive medications, including their effectiveness and tolerability • Adherence to therapy • Past history of HT during pregnancy/pre-eclampsia/eclampsia
Risk factors
• Family history of hypertension, especially in grade one relatives <50 years of age • Family history of renal disease and premature atherosclerosis (in men <55 years of age, in women <65 years of age) • Smoking, including e-cigarettes — currently and in the past — number of pack-years • Inappropriate diet, amount of salt intake, alcohol consumption — amount and type • Lack of regular physical activity/sedentary lifestyle • Increase or loss of weight in the past • Erectile dysfunction • Sleep disturbance: sleep length and quality, snoring, sleep apnea (information also from the partner) • Stress related to work or personal life (subjective stress level) • In women, premature menopause (natural/iatrogenic) • Low weight at birth, premature birth • Pregnancy-related events — recurrent miscarriages, stillbirths • Chronic inflammatory diseases, frequent and prolonged infections, especially COVID-19 and influenza • Long-term oncological treatment
History and symptoms of HMODs, cardiovascular diseases, strokes and kidney disease
• Brain and eyes: headache, dizziness, fainting, visual impairment, TIA, sensory or motor deficits, stroke, carotid revascularisation, cognitive function impairment, memory impairment, dementia (in older people) • Heart: chest pain, dyspnea, syncope, peripheral edema, history of myocardial infarction, coronary revascularisation, symptoms or diagnosis of arrhythmia (especially atrial fibrillation), heart failure • Kidney: thirst, polyuria, nycturia, hematuria, recurrent urinary tract infections, patient or family history of CKD (e.g. polycystic kidney disease), history of urological surgery, congenital abnormalities of the urinary tract (in young patients), overuse of NSAIDs. • Peripheral arteries: cold extremities — observed asymmetry of temperature and/or skin colour, intermittent claudication (painless claudication, pain at rest), ulceration or necrosis of the skin of the lower limbs, previous peripheral revascularisation
Assessment for secondary HT
• Young age of onset of HT (<40 years of age) and >160 mm Hg systolic BP values or sudden development of HT or rapidly deteriorating BP control in older patients • Recurrent renal/urinary tract diseases • Paroxysmal symptoms suggestive of pheochromocytoma • History of spontaneous or diuretic-induced hypokalemia, episodes of weakness/painful muscle cramps (hyperaldosteronism) • Recurrent elevated BP with pulmonary edema with unstable renal function parameters (renal artery stenosis) • Symptoms suggestive of thyroid disease or hyperparathyroidism • Use of hormonal contraception or hormone replacement
Drug treatment (other than antihypertensive drugs)
• Psychostimulant/recreational drug abuse, concomitant therapies, e.g. glucocorticosteroids, including over-the-counter paracetamol, NSAIDs/COX-2 inhibitors, immunosuppressants, anticancer drugs, vasoconstrictors

Abbreviations: COVID-19, coronavirus disease 2019; COX-2, cyclooxygenase 2; HMOD, hypertension-mediated organ damage; NSAIDs, non-steroidal anti-inflammatory drugs; CKD, chronic kidney disease; BP, blood pressure; CV, cardiovascular; TIA, transient ischemic attack

Table 4.2. Essential elements of the physical examination associated with hypertension (HT)

Body structure
• Body weight and height measured on a calibrated scale, with the calculation of BMI • Waist circumference, neck circumference
Symptoms of organ damage caused by HT
• Neurological examination and assessment of cognitive functions • Auscultation of the heart and carotid, renal, femoral arteries • • Palpation of carotid and peripheral arteries
Secondary HT symptoms
• Assessment of skin lesions: café-au-lait spots associated with neurofibromatosis (pheochromocytoma) • Palpation of the kidneys to detect enlargement in polycystic kidney disease • Auscultation of the heart and renal arteries to look for murmurs indicative of aortic stenosis or renovascular HT • Symptoms (phenotypic features) of Cushing's disease or acromegaly • Symptoms of thyroid disease

Abbreviation: BMI, body mass index

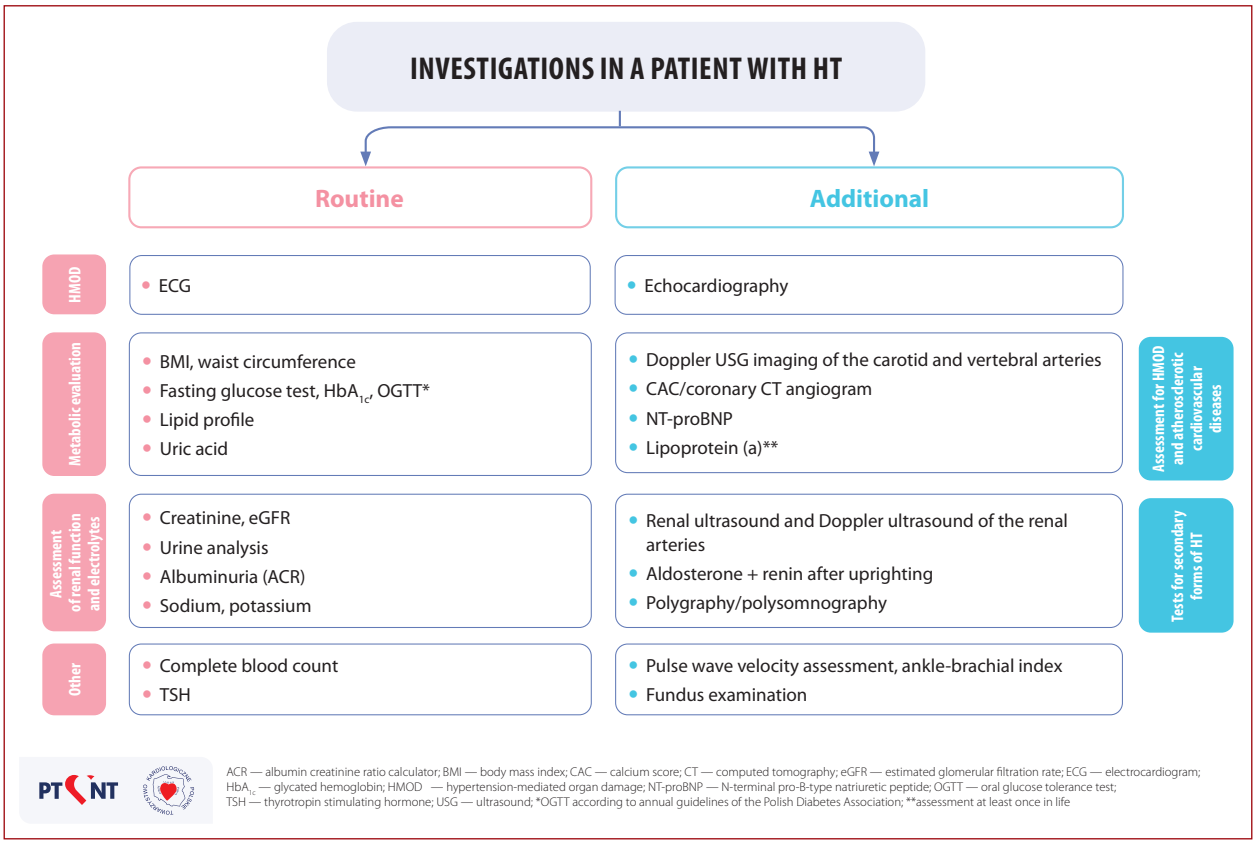


Figure 4.1. Basic and extended medical examinations in a patient with hypertension (HT)

Table 4.3. Basic medical examinations in patients with hypertension (HT)

Routine medical examination	Clinical significance	Frequency
Peripheral blood morphology — hemoglobin and/or hematocrit	Screening for causes of secondary HT (polycythemia, e.g. in the course of sleep apnea, secondary polycythemia, polycythemia vera)	Depending on the results and indications
Fasting glucose test, HbA1c, OGTT*	Cardiovascular risk assessment and comorbidities, diagnosis of diabetes and prediabetes	According to PTD guidelines
Lipoprotein profile: total cholesterol, HDL cholesterol, LDL, non-HDL cholesterol and triglycerides	Cardiovascular risk assessment	In patients on lipid lowering therapy — once a year, in others — according to PTL guidelines
Potassium, serum sodium	Assessment before and after initiation/modification of antihypertensive treatment Screening for secondary HT (hyperaldosteronism, Cushing's disease)	At least annually and after modification of antihypertensive treatment
Serum uric acid	Cardiovascular risk assessment	Depending on obtained results
Serum creatinine to assess eGFR Urine — general examination and mandatory urine albumin to creatinine ratio (ACR)	Cardiovascular and HMOD risk assessment Screening for secondary HT (parenchymal kidney disease, and renal vascular disease) Assessment before and after initiation/modification of antihypertensive treatment	Serum creatinine with eGFR assessment at least once a year and after modification of antihypertensive treatment ACR at least once a year and depending on the results and indications
TSH	Screening for secondary HT — hypothyroidism or hyperthyroidism	Depending on the results and indications
12-lead ECG	Assessment of HMOD (hypertensive heart disease, left ventricular hypertrophy) Assessment of comorbidities (atrial fibrillation, history of myocardial infarction)	Once a year

*OGTT as recommended by PTD

Abbreviations: ACR, albumin creatinine ratio calculator; eGFR, estimated glomerular filtration rate; ECG, electrocardiogram; HbA1c, glycated hemoglobin; HMOD, hypertension-mediated organ damage; HT, hypertension; OGTT, oral glucose tolerance test; PTD, Polish Diabetes Association; PTL, Polish Lipid Association; cardiovascular; TSH, thyrotropin stimulating hormone

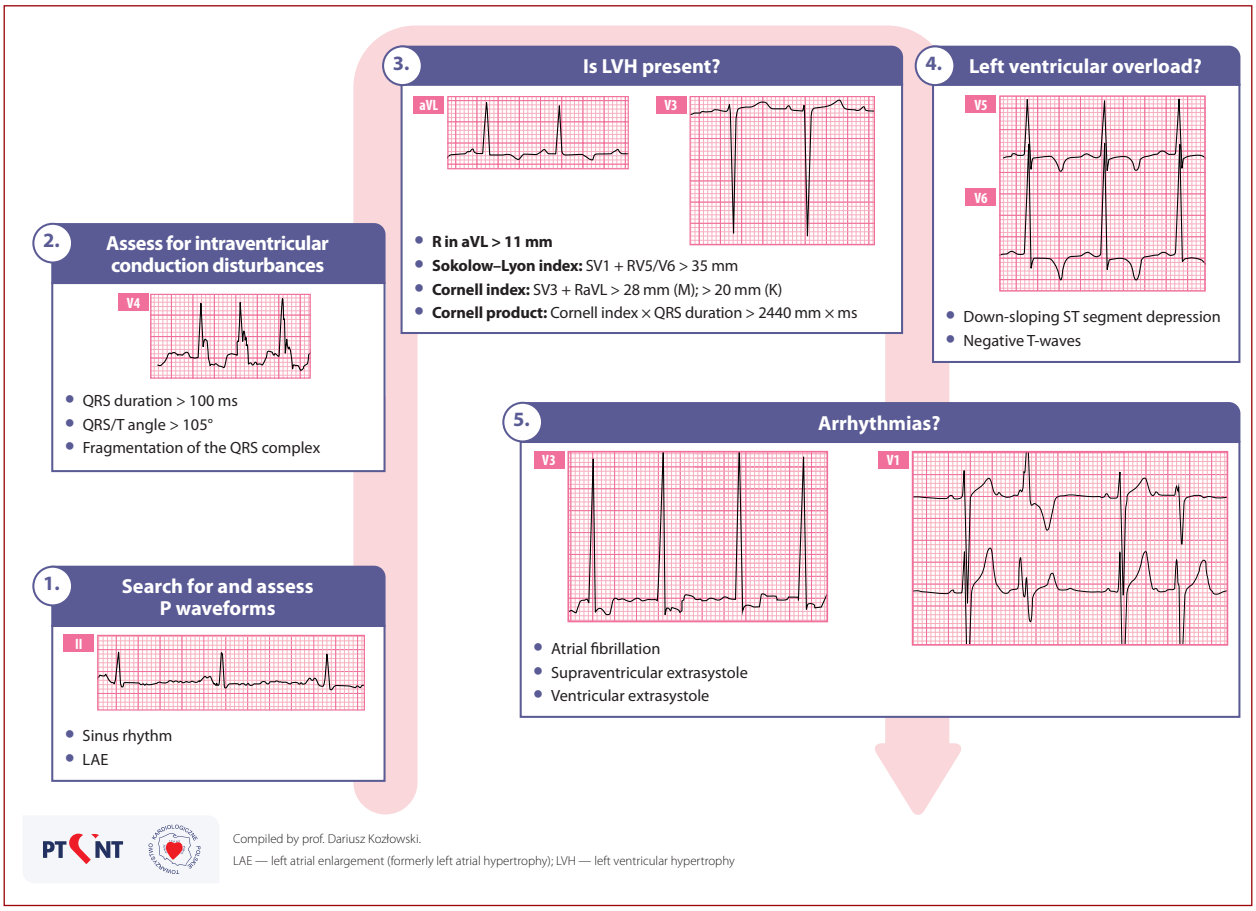


Figure 4.2. Interpretation of an electrocardiographic examination in a patient with hypertension (HT). The criteria for diagnosing left ventricular hypertrophy (LVH) presented in the figure authorise the diagnosis of LVH, i.e. organ damage due to HT, which affects the patient's assessment and prognosis

Additional medical examination

Additional medical examination is to be considered at the initial assessment of a patient with HT, whenever the results may influence further treatment (Figure 4.1). The aim of the examination is primarily to optimise cardiovascular disease risk assessment and to assess HMOD and secondary HT risk [41]. Plasma lipoprotein(a) concentration should be assessed in every adult once in their life [42]. Tests such as non-contrast-enhanced computed tomography (CT) scans to assess calcification index, coronary artery CT scans, ankle-brachial index (ABI), carotid artery ultrasound and echocardiography may document HMOD and confirm the presence of atherosclerotic cardiovascular disease. These test results are important in the risk re-classification (to high or very high risk category) which further justifies the redefinition of therapeutic goals. Based on the results of additional evaluation, the initiation of pharmacotherapy in elevated BP category may be justified.

4.3. Electrocardiographic assessment in a patient with HT

The 12-lead ECG is a key tool in the routine evaluation of patients with HT (Figure 4.2). The development of left ventricular hypertrophy (LVH), a significant HMOD, which becomes more probable along with the duration and severity of HT. ECG recording not only helps to predict cardiovascular risk but also provides valuable information for the clinical assessment of the patient i.e.: detection of atrial fibrillation (AF), history of coronary events. However, the sensitivity of ECG in the diagnosis of LVH is substantially lower as compared to echocardiography.

The Sokolow–Lyon and Cornell indices are key ECG-derived criteria for the diagnosis of LVH. Based on Sokolow–Lyon index criteria, LVH is more commonly diagnosed in people with higher BP, older persons, and males vs. females. In contrast, with reference to the Cornell index criteria, LVH is more common in people with lower BP, younger people, women and obese people. Abnormal ST-segment, and T-wave documented in the lateral precordial leads are the most pronounced signs of LVH. Left ventricular hypertrophy on ECG is a strong indicator of the risk of arrhythmia, including sudden cardiac death (SCD), AF, heart failure and stroke [4].

In addition to the LVH assessment, the ECG provides information on heart rate (HR), type of rhythm, atrioventricular conduction and repolarisation phase disturbances. These data can help to choose an appropriate antihypertensive therapy [4].

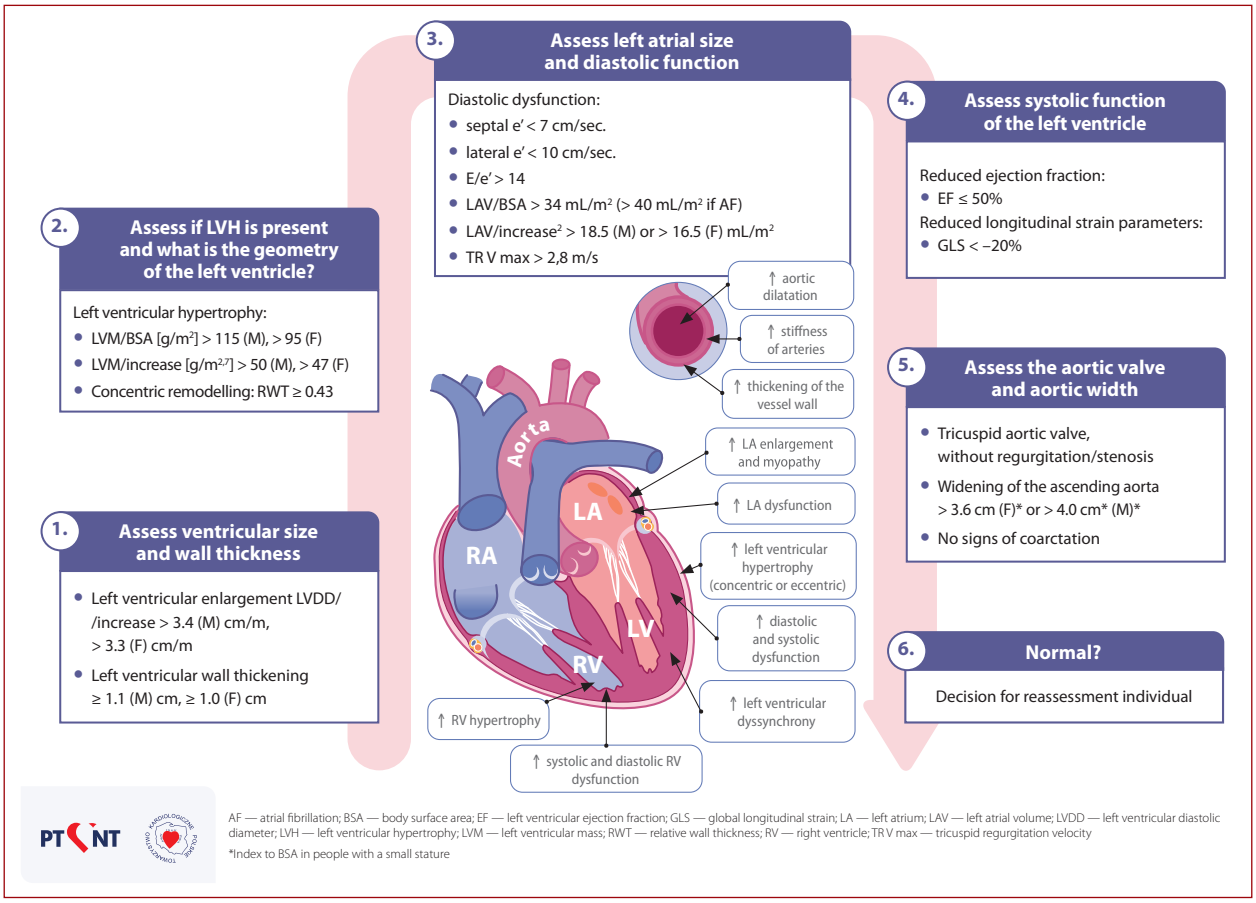


Figure 4.3. Interpretation of an echocardiographic examination in a patient with hypertension (HT) [4, 5, 45]. Abnormal parameters allow for the diagnosis of left ventricular hypertrophy (LVH) (point 2), diastolic dysfunction (point 3) or systolic dysfunction (point 4), i.e. organ damage due to HT, which affects the patient's assessment and prognosis

4.4. Echocardiographic evaluation of a hypertensive patient

Studies show that LVH documented in the echocardiographic examination is an independent risk factor for cardiovascular events, while its regression is associated with a risk reduction [43].

The echocardiographic examination should be considered in all patients with HT. It allows to detect subclinical changes such as LVH, left ventricular remodeling, assessment of systolic and diastolic function, as well as the morphology and function of valves and increased aorta diameter (Figure 4.3). In hypertensive patients with heart murmurs, heart failure symptoms, chest pain, syncope or palpitations, the echocardiographic examination becomes a key diagnostic tool. Occasionally, echocardiography bears the potential to detect secondary forms of HT, such as coarctation of the aorta.

Parameters of left ventricular structure and function considered as subclinical changes in the course of HT (Figure 4.3) are the same as those assessed in patients with heart failure with preserved ejection fraction (HFpEF). This highlights the continuity of cardiovascular risk and the role of HT in the development of clinically overt disease. The basis of diagnosis in such cases is the echocardiographic examination [44].

4.5. Renal function assessment in a patient with HT

Hypertension constitutes the second most common cause of chronic kidney disease (CKD) after diabetes. Inversely, hypertension may also result from primary kidney disease. Deterioration of renal function can be detected by routine laboratory tests using estimated glomelural filtration rate (eGFR) based on either serum creatinine or cystatin C (if available) [46]. Serum creatinine poorly illustrates impaired kidney function, as significant deterioration of renal function can occur with creatinine concentrations remaining within the broad laboratory normal range. Chronic kidney disease is classified based on eGFR, using 2009 CKD-Epidemiology Collaboration formula, and the presence and severity of albuminuria [47, 48]. The albumin–creatinine ratio (ACR) is assessed in a urine sample (preferably in the morning) and is the preferred method for measuring urinary albumin excretion [49]. A single negative strip test result as well as a single normal ACR result do not rule out moderately increased albuminuria [50]. To confirm the diagnosis of moderately or severely increased albuminuria,

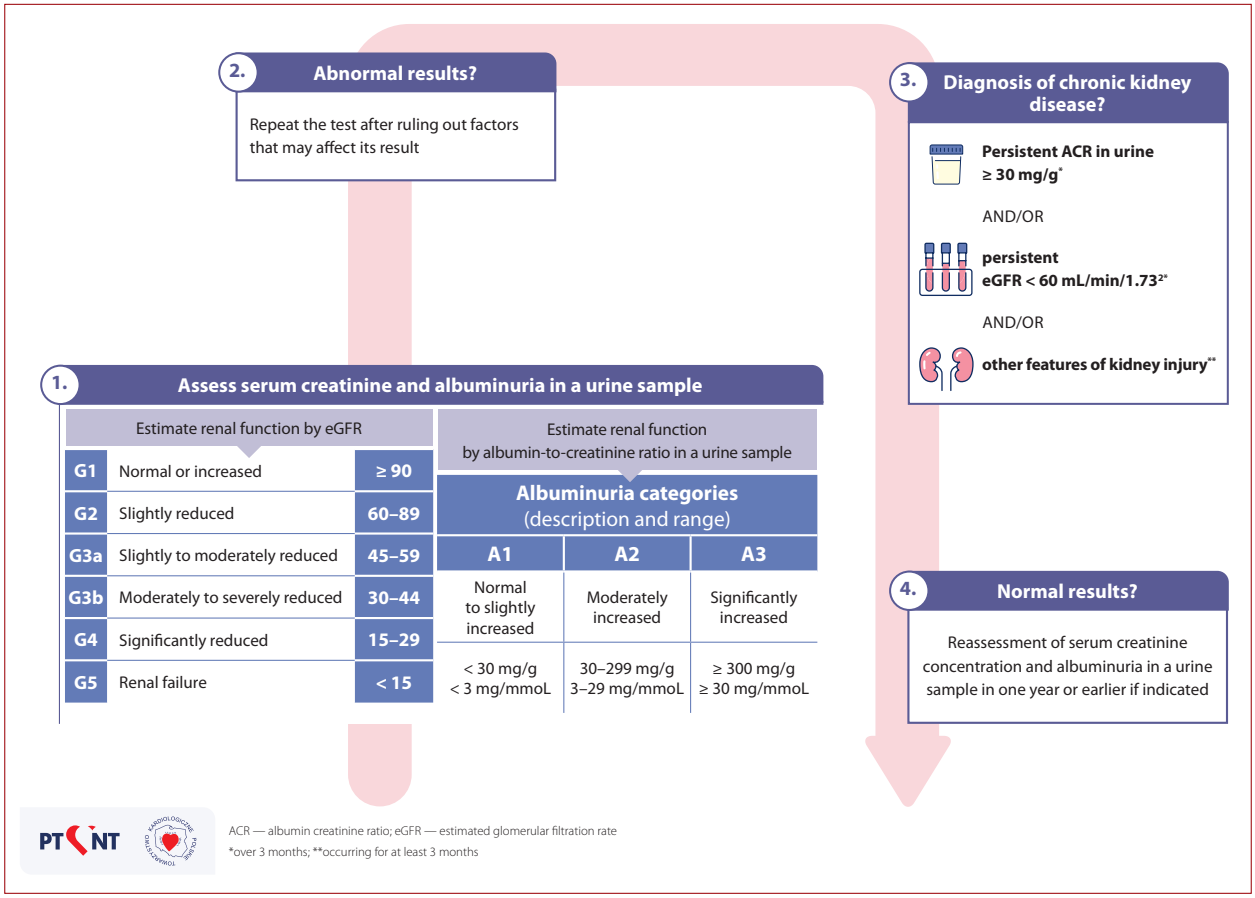


Figure 4.4. Renal function assessment in a patient with hypertension (HT)

two results within this range taken three months apart are required [48]. Serum creatinine, eGFR and ACR should be monitored in all patients with HT (Figure 4.4). The tests should be repeated at least once a year.

Renal ultrasound

Owing to relatively low cost and wide availability renal ultrasound is often utilized to assess kidneys morphology [51, 52]. It is a valuable method for diagnosing CKD and detecting renal artery stenosis [53]. Doppler imaging can be used to assess hemodynamic alterations in the renal artery and the kidney. Doppler spectral ultrasound allows for the measurement of the renal resistive index (RRI), which is a non-invasive and repeatable way to assess the compliance or resistance of the kidneys and systemic arteries [54]. In healthy adults, the RRI ranges from 0.58 to 0.64. A value below 0.7 is considered normal [4, 55]. In relation to age, high RRI values may indicate renal parenchymal disease (e.g. diabetic or hypertensive nephropathy). A difference in RRI between the kidneys may indicate renal artery stenosis [56, 57].

4.6. Other diagnostic tests in a patient with HT

In different settings, hypertensive patients' evaluation may be extended with tests that aim at the HMOD assessment and risk reclassification (HMOD criteria are given in brackets) [2, 5, 58–59]:

- ultrasound examination of the carotid, vertebral or femoral arteries for risk stratification (presence of atherosclerotic plaques, focal wall thickening >1.5 mm);
- assessment of the coronary artery calcification (>100 Agatston score);
- assessment of thyroid-stimulating hormone (TSH);
- N-terminal pro-B-type natriuretic peptide (NT-proBNP) (>125 pg/ml <75 years of age or >450 pg/ml >75 years of age);
- ABI assessment;
- pulse wave velocity (PWV): carotid femoral PWV (cfPWV) >10 m/s and brachial-ankle PWV (baPWV) >14 m/s.

In specific settings, the evaluation of hypertensive patients may be extended to include:

- 24-hour ECG recording (to evaluate arrhythmias);
- fundoscopy (suspition of malignat HT).

4.7. Assessment for secondary forms of HT

Symptoms that may indicate the presence of secondary HT and the screening tests are shown in Figure 4.5. Heart morphology and functional abnormalities specific for secondary forms of HT are also presented.

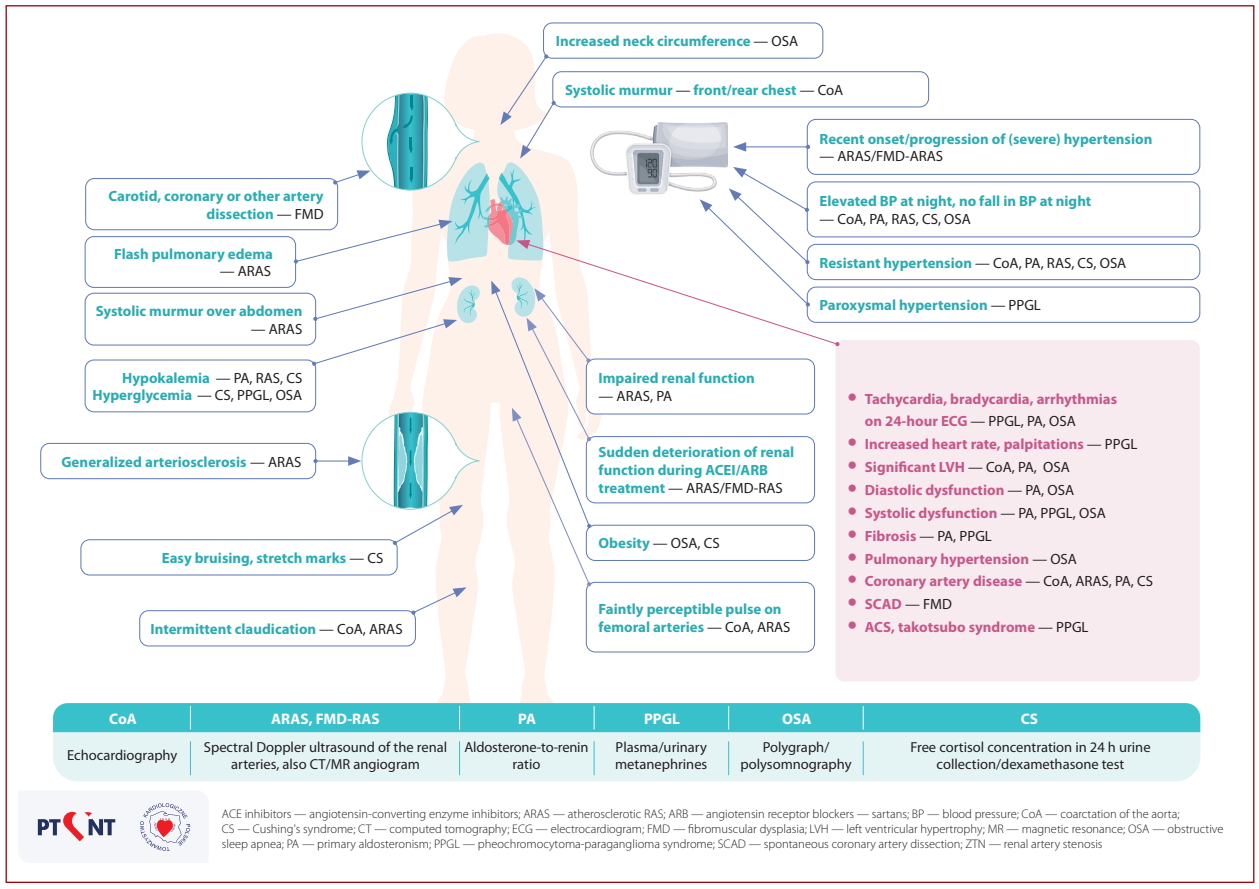


Figure 4.5. Symptoms that may indicate the presence of secondary hypertension (HT) and the screening tests. Based on [4, 5, 60, 61]

5. CARDIOVASCULAR RISK ASSESSMENT IN A PATIENT WITH HT

In most patients, HT coexists with other diseases and risk factors that affect cardiovascular health [62, 63]. In daily practice, priority should be given to patients at high and very high cardiovascular risk. A tool which allows to identify patients at high and very high cardiovascular risk are risk scorecards such as SCORE2, SCORE2-OP, SCORE2-Diabetes, as well as a scale based on "10 for Heart" being developed for the Polish population. We recommend that patients at high and very high cardiovascular risk are identified according to the scorecards, as well as using a range of risk factors and comorbid conditions, as illustrated in Figure 5.1. In patients at high and very high cardiovascular risk, it is essential to take immediate action to substantially reduce the risk, which includes blood lowering pharmacotherapy if BP ranges between 130–139 for systolic BP, and/or 80–89 mm Hg for diastolic BP [4, 25, 41, 42, 64].

In addition to the risk factors shown in Figure 5.1, other risk factors and clinical conditions affecting cardiovascular risk should be considered [4, 65], such as:

- malignant HT/resistant HT;
- increased HR (resting HR >80/min);
- hepatic steatosis;
- chronic obstructive pulmonary disease;
- obstructive sleep apnea (OSA) and other sleep disorders;
- chronic inflammatory disease;
- migraine with aura;
- depressive disorders/chronic stress;
- premature and early menopause;
- frailty;
- other psychosocial and environmental factors (noise and pollution exposure), migration.

6. HYPERTENSION AS A COMPONENT OF THE METABOLIC SYNDROME

Hypertension is one of the most common risk factors for cardiovascular diseases in Poland. In most cases, patients with HT have additional cardiovascular risk factors such as obesity, dyslipidemia or glucose metabolism disorders. In response to that, in 2022, Polish experts proposed a new definitione of metabolic syndrome (MS) [64].

The primary criterion for the diagnosis of MS is obesity as determined by waist circumference and/or BMI. Additional criteria are HT or elevated BP, atherogenic dyslipidemia and pre-diabetes or diabetes. Obesity and two of the three additional criteria allow the diagnosis of MS (Figure 6.1). Waist circumference cut-off values for the diagnosis of abdominal obesity are debated; in

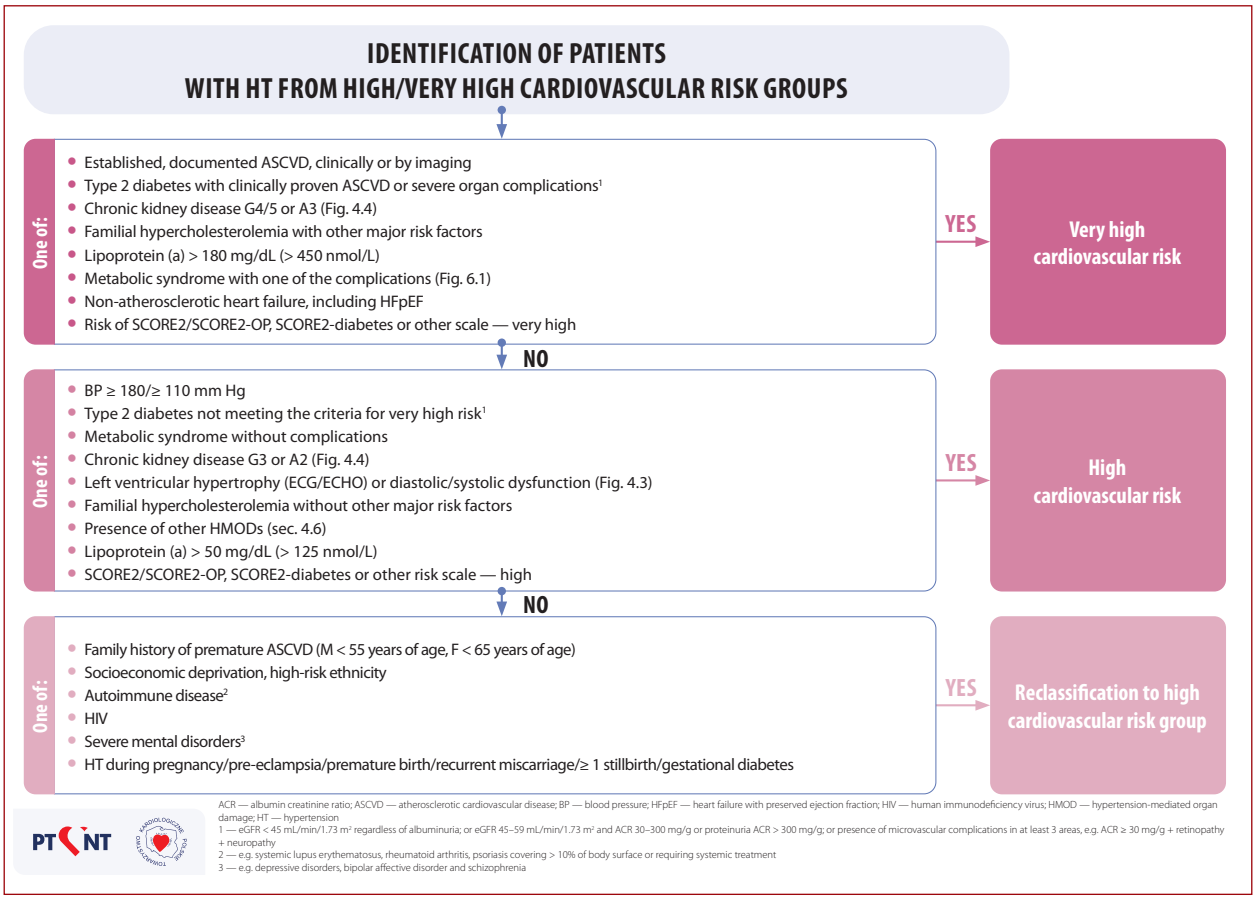


Figure 5.1. Distinction of hypertension (HT) patients at high and very high cardiovascular risk. Developed based on [4, 25, 41, 42, 64]

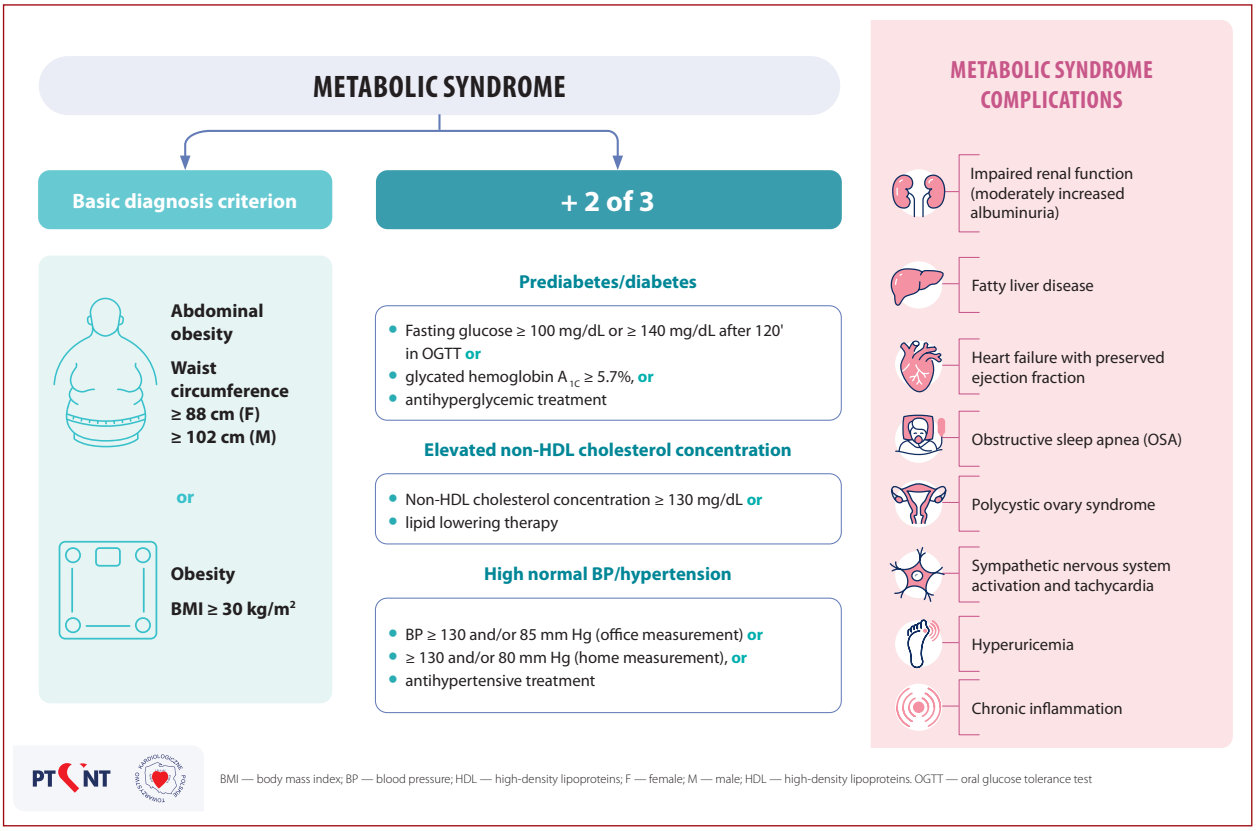


Figure 6.1. Criteria for the diagnosis of metabolic syndrome and its complications. Based on [64]

young people, a waist circumference >80 cm in women and >94 cm in men may already indicate abdominal obesity [64].

The WOBASZ II study shows that 32% of the adult Polish population meets the criteria for the diagnosis of MS [66]. Its most common component is BP ≥130/85 mm Hg or the use of antihypertensive treatment (94% of WOBASZ II participants). Atherogenic dyslipidemia was found in 91% and prediabetes or diabetes in 61% of subjects. The increasing prevalence of obesity may lead to more frequent cases of MS.

Every patient with HT should be assessed for the remaining components of MS. Effective non-pharmacological and pharmacological treatment of each of the four components of MS can substantially reduce cardiovascular risk. Attention should also be paid to complications associated with MS, such as moderately increased albuminuria, hepatic steatosis, OSA or HFpEF, the presence of which further confer cardiovascular risk (Figure 5.1); prevention and treatment of MS reduces the risk of development of abovementioned complications of MS [64].

7. INITIATION OF TREATMENT AND TARGET VALUES

7.1. Initiation of HT treatment

Lowering BP is a key action that significantly reduces cardiovascular risk in patients with HT. Therefore, it is important not to delay the initiation of antihypertensive treatment in patients with a confirmed BP above 140/90 mm Hg [67]. Regardless of baseline BP values, all patients with elevated BP or HT should initiate non-pharmacological measures (section 8) aimed at lowering BP. At the same time, antihypertensive pharmacotherapy should be introduced in all patients with HT and considered in patients with BP within 130–139/80–89 mm Hg who are at high or very high cardiovascular risk after 3 months of non-pharmacological management (Figure 2.2).

7.2. Antihypertensive treatment in patients with elevated BP

The basis of the inclusion of antihypertensive pharmacotherapy in patients with a systolic BP in the range 130–139/80–89 mm Hg is the results of studies showing that such treatment is effective in reducing the risk of developing HT [68–70]. Studies indicate that long-term exposure to elevated BP and other major factors contributing to cardiovascular diseases significantly increases the overall cardiovascular and death risk [71]. It is therefore reasonable to subject patients with elevated BP who are at high or very high cardiovascular risk (criteria in Figure 5.1) to antihypertensive intervention if changes in their lifestyle do not result in BP lowering, despite the lack of hard end-point studies in that group. A decision to introduce pharmacotherapy should be made after 3 months of ineffective non-pharmacological treatment. It is then recommended to start with monotherapy while continuing with the implementation of lifestyle changes (Figure 7.1).

7.3. BP target values

Data from both observational and randomized studies support the recommendation to reduce BP below 130/80 mm Hg, but not lower than 120/70 mm Hg (Figure 7.2) [4, 5, 72, 73]. In this document, the decision-making patterns are simplified, the previous proposals are abandoned in favour of a single, clearer algorithm — it should be assumed that the patient is to be treated considering that goal unless "exceptions" presented later in the section is met. The previous guidelines were revised, the importance of age in determining BP targets was reduced [2]. The basic strategy of pharmacologically lowering systolic BP to 120–129 mm Hg is now recommended for most patients. There are several reasons for that:

- the health status and life expectancy of Poles have improved, thanks to, e.g. better BP control in older people;
- frailty is one of the most common reasons for modifying antihypertensive treatment goals. Therefore, rather than just taking age into account, it is important to consider frailty more broadly. Using only the age criterion leaves out a significant proportion of the population: 6.6% of Poles aged 60–64 may suffer from frailty and 51.7% are at risk of it. In turn, 11.8% of people aged 75–79 are healthy and do not require mitigating therapeutic targets [15]. The assessment for the presence of frailty (using the 9-item Canadian scale or more specific tools) should become a standard at the initial and annual screening of patients at the age of >60.
- the results of intervention studies such as STEP, SPRINT or ESPRIT, which included elderly patients with systolic BP targets below 120 mm Hg, showed a reduction in cardiovascular morbidity and mortality [74–76]. However, the criticism of these studies concerns the enrollment of relatively healthy patients, which does not necessarily reflect the actual health condition of the majority of the elderly population, including in Poland [15]. This confirms that the decision on BP targets should be based on frailty risk and not only on the age of the patient.

Before starting HT pharmacotherapy, it is important to make a clinical decision as to whether the standard target of lowering BP to 120–129/70–79 mm Hg is appropriate for the patient [77]. It is sometimes necessary to set individual, more liberal targets, for example a systolic BP in the range 130–139 mm Hg, in some clinical settings:

- in patients at the age of ≥80;
- when a reduction to 120–129/70–79 mm Hg is not well tolerated; then the rule of thumb is "as low as reasonably achievable" [5];
- in patients with at least mild frailty, regardless of age (in patients with severe/very severe frailty, therapy goals should be determined individually) — see also Figure 11.9;

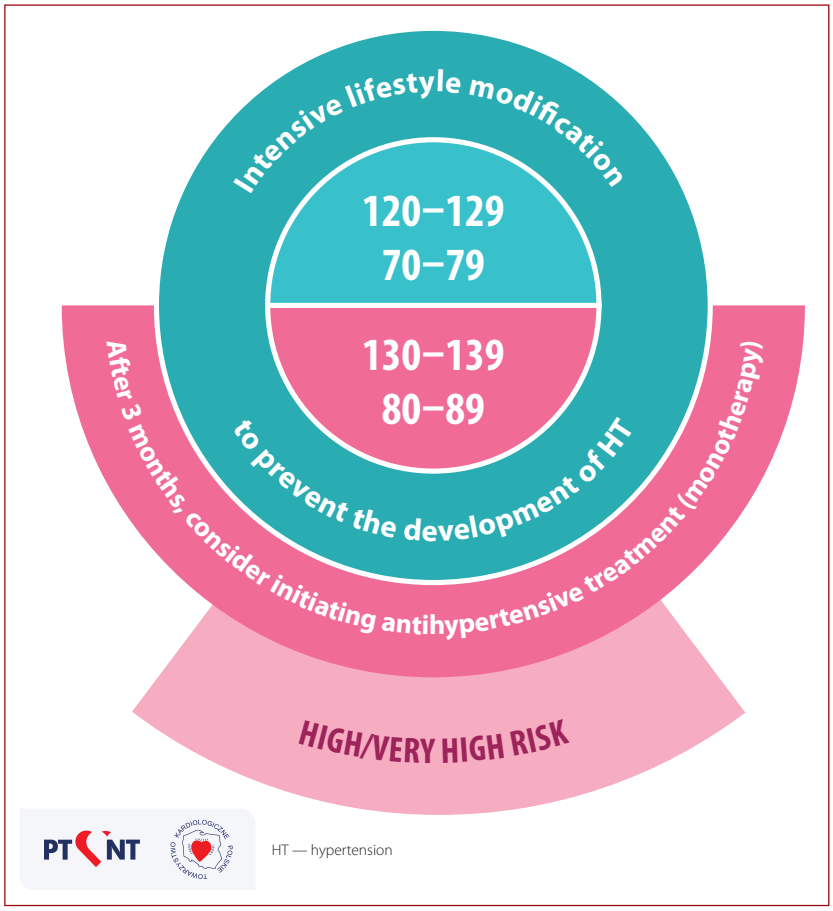


Figure 7.1. Management of patients with elevated blood pressure

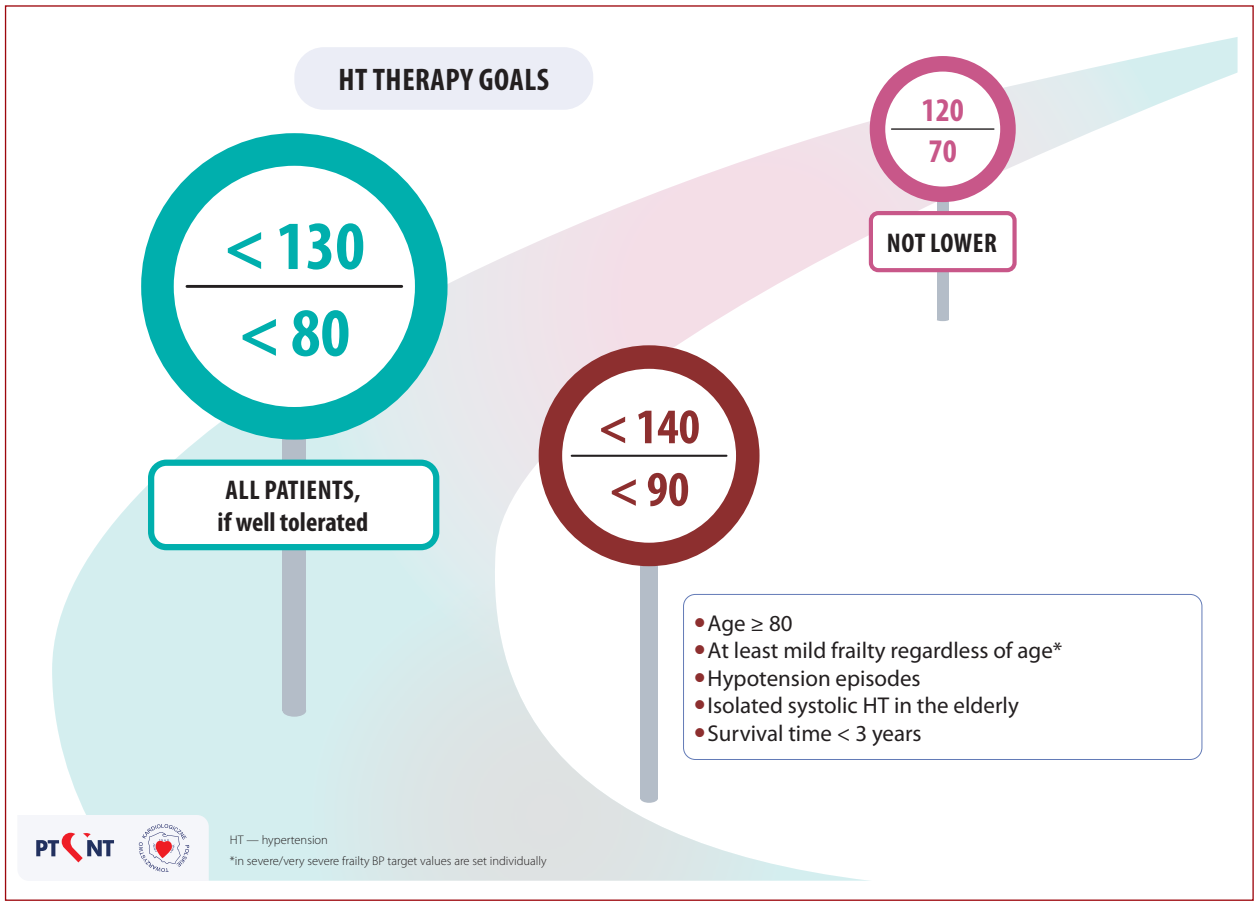


Figure 7.2. Blood pressure (BP) target values

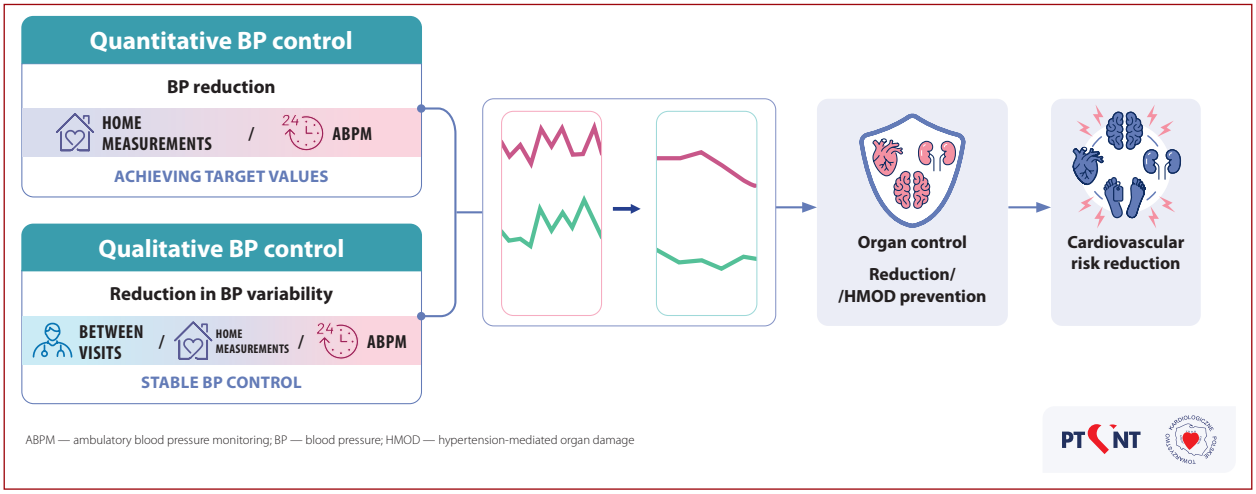


Figure 7.3. Dimensions of antihypertensive effectiveness

- in the case of hypotension syndromes, e.g., orthostatic, post-exercise or postprandial hypotension or occurring during sleep;
- in elderly patients with isolated systolic hypertension (ISH);
- in patients with a life expectancy of less than 3 years.

When it comes to office BP measurements, it is worth follwoing the "trust but verify" principle. This means that, where possible, it is advisable to take BP measurements outside the office before starting therapy and while monitoring its effectiveness [5].

7.4. Dimensions of antihypertensive effectiveness

Achieving target BP is only part of effective HT control. In addition to achieving BP targets ("quantitative" control), the effect of antihypertensive treatment on BP variability ("qualitative" control) — achieving stable HT control — is also important. A growing body of data indicates that increased BP variability in ABPM, home measurements and office measurements (between visits) is associated not only with a higher risk of HMOD and cardiovascular events but also with a higher risk of cognitive impairment (Figure 7.3). Assessing the effect of the treatment used on BP variability is, therefore, an additional exponent of the quality of HT control. Studies show that the use of long-acting antihypertensive drugs may have a beneficial effect on BP variability [78–81].

8. NON-PHARMACOLOGICAL MANAGEMENT IN PATIENTS WITH HT

Non-pharmacological management in patients with HT is a key component of therapy. It is the basis for preventing the development of HT in people with elevated BP. It helps to reduce cardiovascular risk and improves prognosis and quality of life. Lifestyle changes result in lower BP, slow the progression of atherosclerosis and may delay the onset of HMOD and clinical signs of atherosclerosis. Non-pharmacological recommendations (lifestyle measures) with documented efficacy in the treatment of HT are shown in Figure 8.1.

A common belief regarding non-pharmacological management is that coffee consumption should be reduced in patients with HT. Coffee consumption does not increase the risk of HT in the general population. In fact, higher coffee consumption may even lower this risk [82]. Therefore, limiting coffee consumption in HT patients is not necessary. In addition, higher consumption of coffee or tea may reduce the risk of type 2 diabetes [83]. The relationship is different with unfiltered, Turkish-brewed or boiled coffee. It contains higher concentrations of caffestol and kahweol, which may slightly increase serum LDL cholesterol concentrations. However, increased cardiovascular risk was observed in cases of consumption of nine or more such drinks per day [84, 85].

In contrast, the consumption of two or more servings of sugar-sweetened beverages per day is associated with a 35% higher risk of coronary heart disease in women [86]. Consumption of such drinks also increases the risk of all-cause mortality. In children and adolescents, sugar-sweetened beverages raise systolic BP and increase the risk of developing HT [87, 88]. From an early age, sugar-sweetened beverages should not account for more than 10% of daily energy intake.

Excessive alcohol consumption is one of the main causes of premature mortality. Increased alcohol consumption is linearly associated with a higher risk of cancer, liver disease, AF, stroke and HF. Although many scientific societies recommend limiting alcohol consumption and set limits, there is no proven safe amount of alcohol for the general population. Findings show a strong linear correlation between alcohol consumption and higher BP, while also suggesting that low consumption may be associated with a lower cardiovascular risk than total abstinence. However, potential cardioprotective benefits may arise from the overall healthier lifestyle of moderate alcohol drinkers. The risk of HT increases in both sexes when daily consumption is one to two drinks, or 10–20 g of alcohol. Reducing alco-

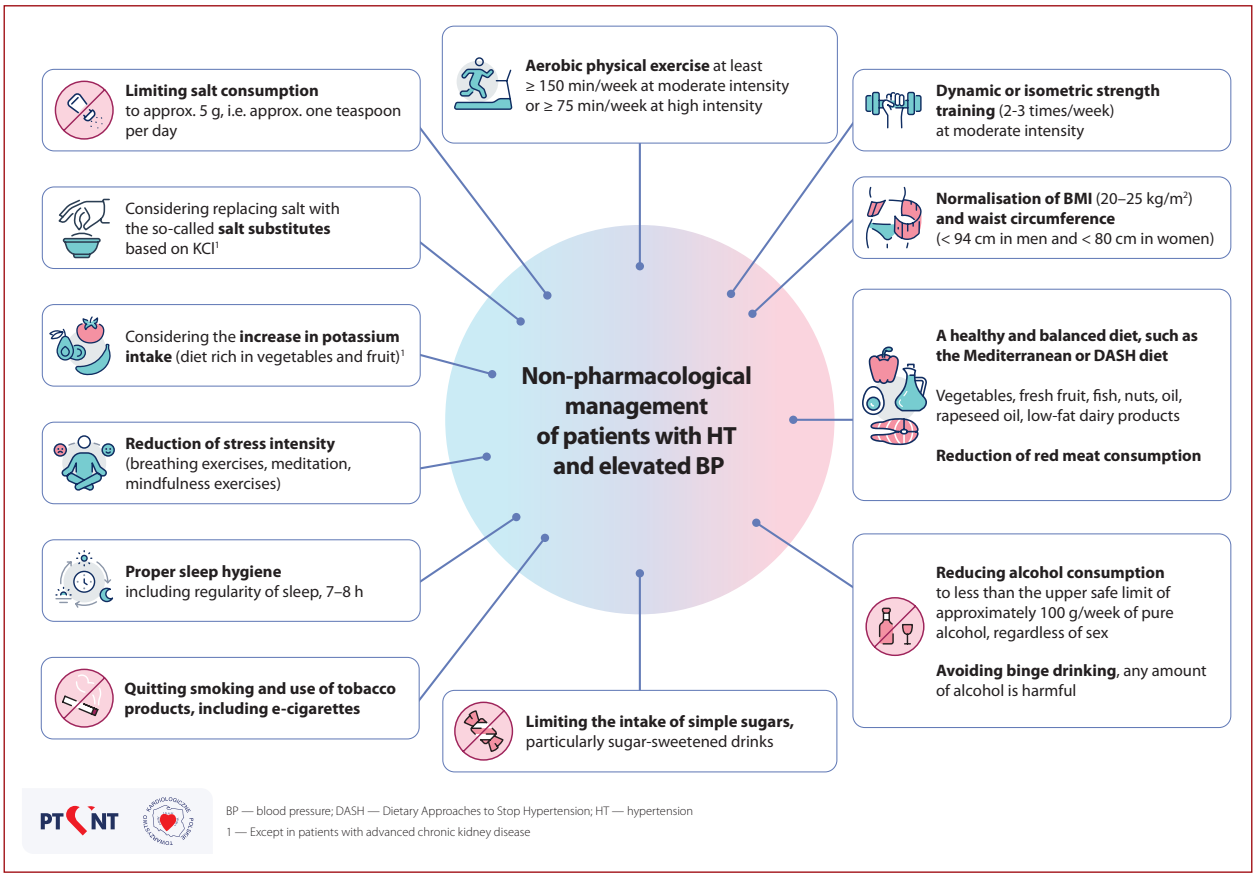


Figure 8.1. Non-pharmacological (changing lifestyle) recommendations with documented efficacy in the treatment of hypertension (HT). Developed based on [4, 5, 41]

hol consumption close to abstinence can lower systolic and diastolic BP by 3.3 and 2.0 mm Hg. Binge drinking is particularly dangerous and, together with uncontrolled HT, it increases the risk of hemorrhagic stroke. Reducing or stopping alcohol consumption, especially in Poland, is recommended for better BP control and overall health [89, 90].

9. BASIC ALGORITHM FOR THE TREATMENT OF HT

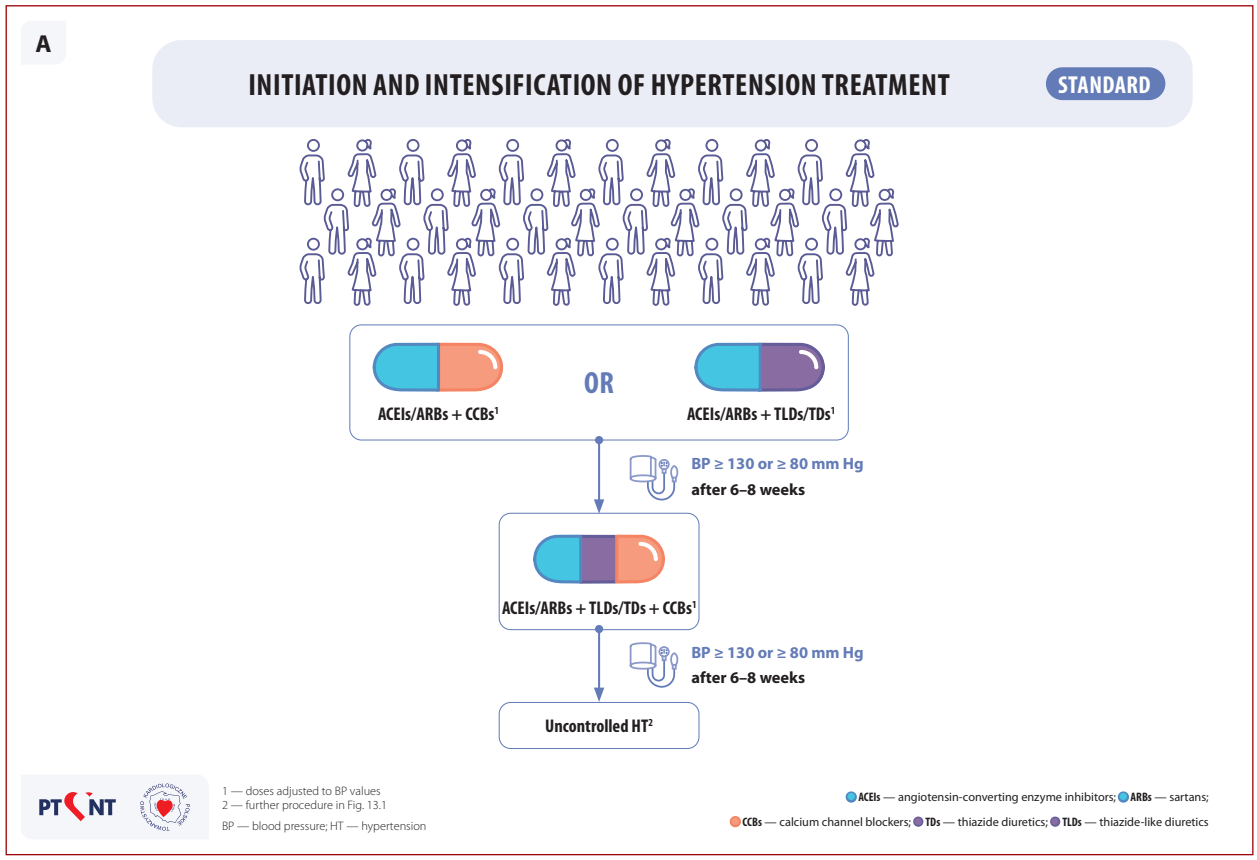
Most antihypertensive drugs used in monotherapy lower BP by less than 20/10 mm Hg and only in approximately half of patients. For that reason, most people with HT require combination therapy. Due to the limited efficacy of monotherapy, it is recommended to start HT therapy with combination therapy, preferably in the form of SPCs. Exceptions are patients in poor general condition, with at least mild frailty (Figure 11.9) or with no HT but with elevated BP, in whom the treatment decision is made on an individual basis, generally starting with monotherapy (Figure 9.1). One to two months after starting two-drug therapy its effectiveness should be assessed and, if target BP values are not achieved, intensification should be considered by adding a third drug to achieve target BP values within three months [2–6, 58, 91]. In recent years, data has been published indicating the effectiveness and safety of starting therapy with a combination of three or four antihypertensive drugs, including the use of SPCs, at low or very low doses. However, this regimen cannot currently be recommended as a routine in daily practice [92].

The use of appropriately selected combinations of two or three drugs, especially in the form of SPCs, can control BP in most patients. The treatment algorithm based on SPCs is effective and better tolerated, promotes patient cooperation and ensures rapid achievement of BP targets. This reduces cardiovascular risk, which is a key goal of HT therapy [2–6, 58, 91, 93].

Groups of antihypertensive drugs that effectively reduce the incidence of cardiovascular events are angiotensin-converting enzyme inhibitors (ACEIs)/angiotensin II receptor AT1 blockers (ARBs, also known as sartans), calcium channel blockers[1] (CCBs), thiazide-like diuretics/thiazide diuretics (TLDs/TDs) and beta-blockers (BBs). The first three groups (the so-called "basic three") are recommended as first-line solutions for the initiation of HT therapy due to their superior efficacy in reducing cardiovascular risk [2–6, 58, 91]. It should be noted that in Poland, among patients using two or three antihypertensive drugs, only 34% use a regimen based on the recommended combinations [12].

The basic treatment strategy should include (Figure 9.1) [2–6, 58, 91]:

[1]For simplicity, unless otherwise stated in the document, the term CCB refers to dihydropyridine CCBs



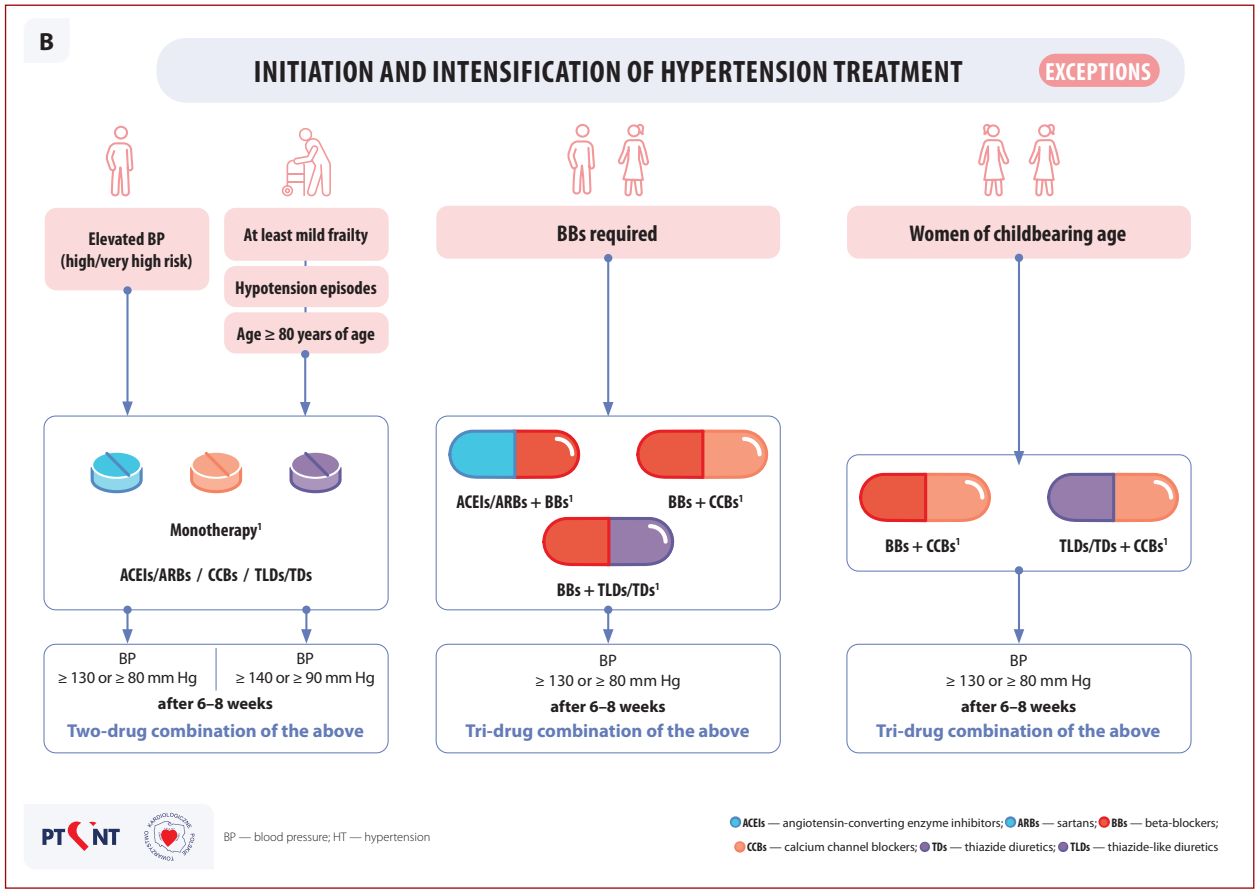


Figure 9.1. Basic strategy for the treatment of hypertension (HT) (**A**) and exceptions to this strategy (**B**)

- ACEIs or ARBs with CCBs or TLDs/TDs (step 1);
- ACEIs or ARBs and CCBs and TLDs/TDs (step 2).

Beta-blockers should be used in selected clinical situations in combination with other drugs or independently of the use of the "basic three" (section 10). When choosing drugs, one should take into account their ability to significantly lower BP, reduce its variability and reduce the risk of developing or worsening HMOD and cardiovascular diseases, as well as their tolerability profile [2–6, 58, 91]. Exceptions to the use of the „basic three" are shown in Figure 9.1.

9.1. Dosage of antihypertensive drugs versus intensification of therapy

As part of the basic algorithm of HT therapy, two approaches to the selection and intensification of doses of antihypertensive drugs are proposed. The first involves starting with lower doses of a two-drug combination, increasing them to maximum doses and then adding a third drug. The second involves starting therapy with low doses of two drugs and moving on to three drugs in low doses. Based on a practical approach in daily practice, it is recommended:

- the use of SPCs at every stage of therapy — the wide availability of doses and combinations allows to modify the doses and numer of drugs while still remaining on SPCs, which translates into better therapeutic persistence [2–6, 58, 91, 94–96]. In the search for available drug combinations in the form of SPCs in Poland, an app developed by PTNT is helpful — mniejlekow.pl;
- matching doses to the patient's BP values and following the principle that adding another drug is more effective than increasing the doses of the drugs already in use [91, 95, 97–100];
- avoiding increasing doses of drugs such as CCBs, as this may increase the risk of side effects [101];
- taking advantage of the benefits of increasing doses of TLDs/TDs when diuretic treatment needs to be intensified, especially indapamide and chlortalidone [92, 102, 103];
- using full doses of ACEIs/ARBs, especially in patients with cardiovascular disease based on atheromatosis or CKD, in line with data from large clinical trials [104–106].

When to use antihypertensive drugs: in the morning or evening?

- With regard to long-acting antihypertensive drugs, no differences have been reported in terms of efficacy in lowering BP depending on whether they are administered in the morning or evening. Randomized trials indicate that there is no difference in the reduction of cardiovascular risk between morning and evening drug administration [107–110].
- However, the use of medication in the evening may be associated with a higher rate of skipping it compared to taking the drugs in the morning. It is recommended to use long-acting drugs once a day, in the form of SPCs, and adjust the time of taking drugs to the patient's habits. The most frequently chosen time is the morning hours [109, 110].
- The TIME study showed no difference in the rate of glaucoma-related hospitalisations, but it did not thoroughly analyse glaucoma-related complications. In the BED-MED study, in turn, glaucoma was an exclusion criterion. Therefore, the administration of antihypertensive drugs in the evening should be avoided in patients with glaucoma [109–112].
- In patients with elevated BP at night, an increase in the dose of diuretic in the morning may be considered, especially in cases of coexisting CKD, diabetes or OSA. In the case of OSA, a mineralocorticoid receptor antagonist (MRA) and/or BBs may also be considered [113, 114].

10. THE PLACE OF BETA-BLOCKERS IN HT THERAPY

In previous guidelines, BBs were mainly recommended for exceptional indications [2, 6]. Despite this, BBs are the most commonly used group of antihypertensive drugs in Poland [12]. Numerous studies have shown that BBs significantly reduce the risk of HF and serious cardiovascular events in HT patients compared with placebo. BBs are also comparatively effective in preventing serious CV events, as are other classes of antihypertensive drugs. The exception is stroke prevention, where they are less effective. This difference may be due to small differences in the BP achieved, including central systolic BP, which has a particular impact on cerebrovascular events [115–119].

Beta-blockers are a diverse group of drugs. Of particular interest are their beta1 selectivity and vasodilatory properties. Studies on nebivolol (additional vasodilatory effect) and bisoprolol, which have higher beta-1 selectivity, showed that these drugs have a more favourable side-effect profile, including a lower incidence of erectile dysfunction [120–122]. Studies using carvedilol, bisoprolol, metoprolol succinate and nebivolol have confirmed their beneficial effects on prognosis in patients with HFrEF [123]. Beta-blockers such as metoprolol and bisoprolol are also effective in treating cardiac arrhythmias. In addition, metoprolol and propranolol are used for non-cardiac conditions such as essential tremor, prevention of migraine attacks or psychosomatic disorders [4, 116, 124].

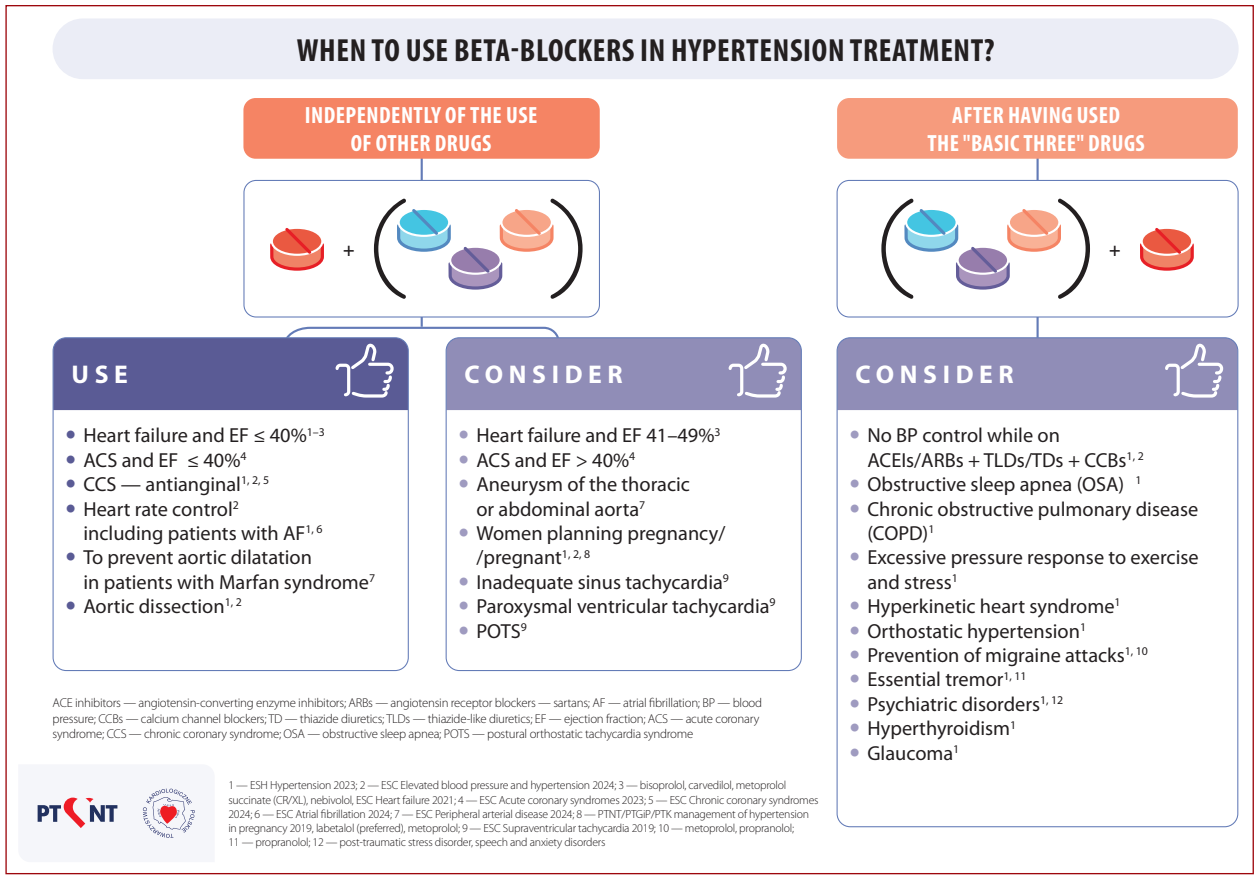


Figure 10.1. Use of beta-blockers (BBs) in hypertension (HT) treatment

A resting HR above 80 beats per minute is common in HT and indicates increased sympathetic nervous system activity [125]. An increase in resting HR is directly associated with a higher risk of AF, HF and increased mortality, both in the general population and in patients with HT. Although the evidence for the benefit of lowering HR in HT is mainly based on post hoc analyses, some data suggest that patients with HT and elevated HR may particularly benefit from BB therapy [124, 126–128]. The use of BBs in HT therapy is illustrated in Figure 10.1 by introducing a three-category division: (1) BBs should or (2) can be considered in specific clinical situations, independent of other drugs, and (3) BBs can be considered after the basic three antihypertensive drugs (ACEIs/ARBs, CCBs and TLDs/TDs) have been used as primary therapy [4, 58].

11. DIFFERENCES IN HYPERTENSION MANAGEMENT

11.1. Hypertension in women

Hypertension in women is associated with a higher risk of myocardial infarction than in men at comparable BP values. Women are more likely to develop concentric LVH and HFpEF and have a higher risk of developing renal failure [129, 130]. Women are also more likely to report adverse effects of antihypertensive drugs, such as edema, cough, hyponatremia and hypokalemia. Although they are more likely to start treatment, it is less likely to be effective. Treatment regimens for HT in women vary according to the patient's age, reproductive plans and metabolic and hemodynamic profile (Figure 11.1).

Hypertension in women of childbearing age

When taking a medical history, attention should be paid to female-specific risk factors such as early menarche, menstrual disorders, polycystic ovary syndrome (PCOS) features, history of pregnancy and use of oral contraceptives (OCs). The clinical assessment should also consider the secondary causes of HT, like fibromuscular dysplasia (FMD) or primary hyperaldosteronism (PA), as well as the quantive assessment of proteinuria [131].

The drug choice in this patients group includes CCBs, BBs and TLDs/TDs. It is recommended to start treatment with a two-drug combination therapy using SPCs (Figure 9.1).

The use of ACEIs, ARBs and MRAs in uncomplicated HT is not recommended due to their teratogenicity. The prescription of these drugs should be limited to female patients with diabetic kidney disease, hypertensive nephropathy, or heart failure, with the provision of effective contraception methods. Patients should be informed about the risks and give their informed consent.

If a woman with HT is planning a pregnancy, her treatment may be continued or changed to drugs dedicated

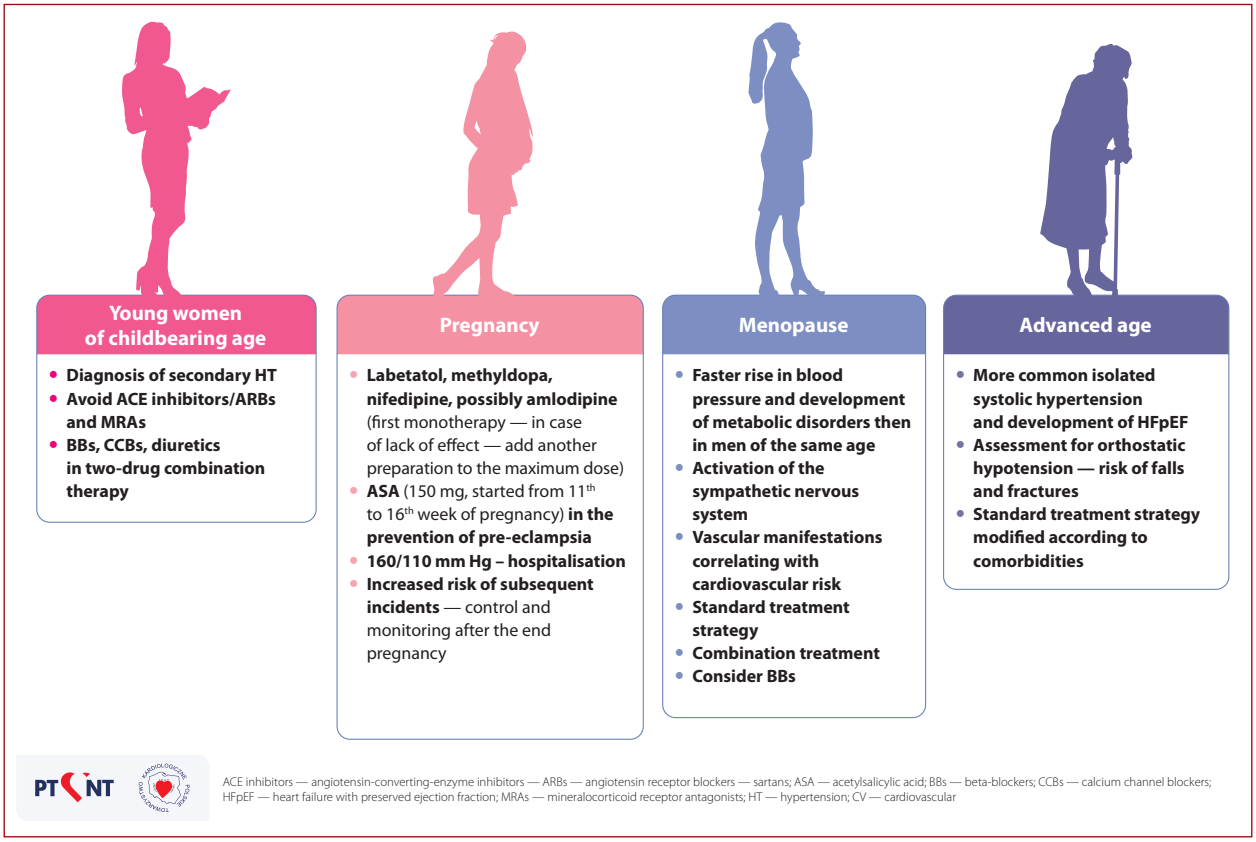


Figure 11.1. Hypertension (HT) management in women by age

to hypertension treatment during pregnancy, such as labetalol, metoprolol, methyldopa or extended-release nifedipine (possibly amlodipine). This is particularly recommended for women planning to use assisted reproduction technologies, as in vitro fertilisation may increase the risk of developing pre-eclampsia (PE) and gestational HT [132].

Oral contraceptives may slightly elevate BP by an average of 5 mm Hg, which applies to systolic and diastolic BP. It is estimated that 2% of women using OCs for four years may develop HT. Their use is also associated with a higher thromboembolic risk and a slight increase in the risk of arterial thrombosis. The described relationship depends on other risk factors present in the patient [133].

A patient using oral contraceptives develops HT: how to manage her?

It is recommended to discontinue oral contraceptives, as it usually lowers BP, and to consider other contraceptives. If BP does not return to normal within three to six months, a comprehensive diagnostic evaluation for HT is required. The initiation of treatment depends on the patient's overall cardiovascular risk.

Menopause

After menopause, BP in women increases more rapidly than in men of the same age. Vasomotor symptoms may indicate future cardiovascular risk [135]. Activation of the sympathetic nervous system plays a role in the pathogenesis of HT and vasomotor symptoms. Patients may benefit from combining ACEIs/ARBs with BBs.

Postmenopausal treatment of HT in women is similar to that used in men and based on the individual characteristics of the patient, such as metabolic and hemodynamic profile and concomitant diseases.

HRT may be used to relieve the menopausal symptoms in women with HT, but it is not

recomended for primary prevention of cardiovascular diseases. It does not affect BP but may improve lipid profile and endothelial function. HRT is contraindicated in women after cardiovascular events and at high thrombotic risk.

What contraceptive can be used in a patient with chronic HT?

Progestogen-only pills are safe for women with well-controlled HT as they do not affect BP [134].

Combined oral contraceptive pills can be used if more suitable methods are not available or acceptable. The risk of cardiovascular diseases depends on the dose of estrogen and risk factors such as obesity, smoking and lipid disorders. They should not be used by women over 35 who smoke, patients with diagnosed cardiovascular diseases, uncontrolled HT or those at very high risk of cardiovascular diseases [45].

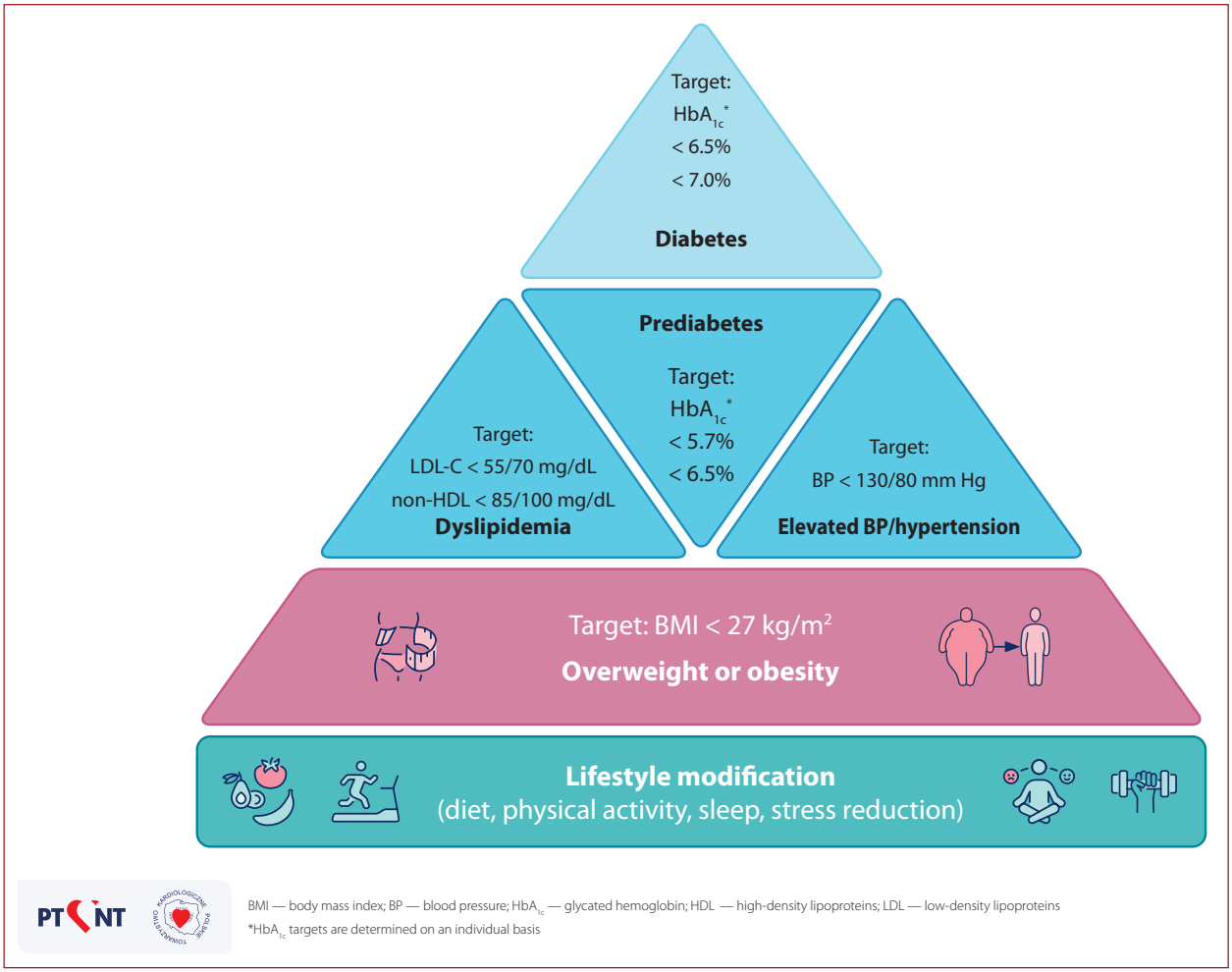


Figure 11.2. Therapy goals of hypertension (HT) and comorbid conditions on the continuum of obesity → metabolic syndrome → diabetes → HFpEF

Intrauterine devices (with copper or levonorgestrel) are an effective and safe option for women with HT. **Progestogen-only subdermal implants** (e.g. etonogestrel), effective for three years, are also a good alternative.

11.2. The "metabolic" patient with hypertension on a continuum of obesity → MS → diabetes → HFpEF

Obesity is a significant gateway to the development of cardiovascular diseases. One of its first consequences is the development of HT, prediabetes, diabetes and atherogenic dyslipidemia [64]. These early complications of obesity, which are the main risk factors for cardiovascular disease, make up MS. This leads to further sequelae of obesity, such as LVH, moderately increased albuminuria, hepatic steatosis and OSA. Left ventricular diastolic dysfunction also occurs, which can result in AF and HFpEF.

This sequence of adverse events can be referred to as the obesity cardiovascular continuum, in which treatment of obesity is crucial (Figure 11.2). The processes along the chain of obesity → MS → diabetes → HFpEF may progress at different rates. Therefore, these patients require an individualized approach to treating HT, taking into account the different severity of obesity complications.

Heart failure with preserved ejection fraction can be considered one of the sequelae of obesity-induced MS [64]. Metabolic syndrome is a significant risk factor for HFpEF. Hypertension leads to concentric LVH (with reduced compliance), and obesity and metabolic disorders, through inflammation and microcirculatory dysfunction, exacerbate left ventricular diastolic dysfunction [64].

Heart failure with preserved ejection fraction is not a homogeneous condition. One can differentiate between its phenotypes associated with obesity and MS and those associated with older age, arterial stiffness or CKD. The co-occurrence of obesity and HFpEF increases the risk of hospitalisation for HF exacerbations [136].

The treatment of obesity improves HT and diabetes control, which is evidence of the importance of the sequence of events outlined above. Reducing the BMI by 10 kg/m^2, for example, through bariatric surgery, allows

some patients with HT to achieve normal BP without antihypertensive medication [137, 138]. Recent studies indicate that bariatric surgery reduces the incidence of AF episodes, and pharmacological treatment of obesity improves exercise tolerance in patients with HFpEF and reduces the severity of OSA [139–141].

Management of the patient in the continuum of obesity → MS → diabetes → HFpEF is based on intensive implementation of lifestyle modification principles and measures to achieve treatment goals in four dimensions: (1) weight reduction, (2) glycemic control, (3) BP reduction and (4) control of serum LDL and non-HDL cholesterol levels (Figure 11.2) [64, 142–145].

Obesity treatment

- To reduce body weight by approximately 0.5 kg per week, it is recommended to introduce a balanced calorie-restricted diet with a daily defficit of 500 kcal to daily requirements. In patients with obesity with concomitant HT, the treatment goal is to reduce body weight by at least 5%–15%. In patients with coexisting prediabetes and diabetes, the goal is to reduce body weight respectively by at least 10% and 5%–15% [64, 146].
- Pharmacotherapy is an obesity treatment option for patients with a BMI ≥30 kg/m^2 who have not achieved significant weight reduction or therapeutic goals through dietary and behavioural management and for overweight patients with a BMI of 27–29.9 kg/m^2 and the coexistence of at least one obesity-related disease [64, 146].
- Five drugs are registered for treating obesity: orlistat, a combination of naltrexone hydrochloride and bupropion hydrochloride; liraglutide; semaglutide and tirzepatide [64, 146].
- In patients with obesity and HT, especially those with MS and its complications, liraglutide, semaglutide or tirzepatide are worth trying because of their BP-lowering effects. The choice of drug should depend on the need for the drug efficacy and the expected therapy outcomes. In patients with cardiovascular disease, semaglutide at a target dose of 2.4 mg/week should be considered first and foremost, as it has been shown to reduce the incidence of serious cardiovascular events. In patients experiencing emotional eating or planning to quit smoking at the same time, naltrexone therapy with bupropion may be considered as an initial treatment. Pharmacological treatment of obesity should be part of a management plan that includes lifestyle modification and changes in eating habits [146–148].
- In a study involving obese patients, 36% of whom had HT, the use of semaglutide reduced BMI by 5.5 kg/m^2, resulting in a 7 mm Hg reduction in systolic BP [149]. Further analysis of studies with semaglutide indicates that a 15% BMI reduction was associated with a decrease in systolic BP of approximately 5 mm Hg. In patients with HT, including resistant HT, such an effect is additionally observed with a reduction in the intensity of antihypertensive treatment [150]. In another study with tirzepatide, involving patients with BP below 140/90 mm Hg, a significant dose-dependent reduction in systolic daytime and night-time BP of 7–11 mm Hg and 6–9 mm Hg in ABPM was observed throughout antihypertensive therapy. This effect was 70% associated with a reduction in body weight [151]. In addition, it has been shown that in patients with moderate-to-severe OSA, a 16%–17% reduction in body weight as a result of tirzepatide therapy led to a 48%–56% apnea-hypopnea index (AHI) reduction, a decrease in OSA severity to a level not requiring continuous positive airway pressure (CPAP) therapy in 42%–50% of patients, and a significant reduction in BP [139].
- Qualification for bariatric surgery based on BMI applies to patients with a BMI >40 kg/m^2 and with a BMI of 35–39.9 kg/m^2 with at least one obesity-related disease (e.g. type 2 diabetes, HT, severe joint disorders, lipid disorders, acute OSA) [146].
- A 5% reduction of body mass, over three months of treatment with a full therapeutic dose, confirms the efficacy of pharmacotherapy [64, 146].

Treatment of prediabetes/diabetes

- Lifestyle modifications, including changes in dietary habits and increased physical activity, are recommended for patients with prediabetes, regardless of their BMI [152]. In patients with a BMI ≥35 kg/m^2, those under 60 and women with gestational diabetes in their history, treatment with metformin for the prevention of type 2 diabetes should be considered [64, 153]. In addition, glucagon-like peptide-1 (GLP-1) receptor agonists or dual GLP-1 and glucose-dependent insulinotropic polypeptide (GIP) receptor agonists, registered for the treatment of overweight and obesity, can be used in patients with a BMI ≥27 kg/m^2 to reduce the risk of progression of prediabetes to type 2 diabetes [154].
- According to the guidelines of the Polish Diabetes Association, metformin is the base of pharmacotherapy in patients with type 2 diabetes. In the case of coexisting overweight and obesity, cardiovascular disease, HF, CKD or very high cardiovascular risk, at the treatment initiation, drugs with proven beneficial effects on cardiovascular risk from the GLP-1 receptor agonist group or dual GLP-1 and GIP receptor agonists or sodium-glucose cotransporter 2 (SGLT2) inhibitors should be added to it [153].
- In patients with type 2 diabetes and atherosclerotic cardiovascular disease, the use of SGLT2 inhibitors and/or GLP-1 receptor agonists is recommended to reduce cardiovascular risk independently of the antihyperglycemic drugs used and the level of glycemic control [25].
- The use of GLP-1 receptor agonists or dual GLP1 and GIP receptor agonists, as well as SGLT2 inhibitors, is associated with BP reduction. Meta-analyses indicate

Table 11.1. Characteristics of hypertension (HT) in patients on the continuum of obesity → MS → diabetes → HFpEF and implications for HT management. Developed based on [64, 142–145, 187]

Characteristics of HT in "metabolic" patients on the continuum of obesity → MS → diabetes → HFpEF	Impact on management
Larger arm circumference	BP measurement using a wider cuff [usually designated L (32–42 cm) or combining two sizes: M–L (22–42 cm)]
Larger increase in systolic BP, higher pulse pressure*	Combination treatment in virtually all patients, starting therapy with two drugs
Greater BP variability	Use of long-acting drugs
Elevated night-time BP, no drop in night-time BP	Use of long-acting drugs Adequate therapy with TLDs/TDs, MRAs, and, if necessary, loop diuretics Prevention and treatment of OSA
HT sodium sensitivity, hypervolemia	Use of TLDs/TDs
Increased risk of hyperkalemia	Periodic assessment of potassium levels
Orthostatic and postprandial hypotension	Need to assess BP after standing up and after meals, adjust the intensity of pharmacotherapy
Difficulties in achieving HT control, frequent resistant HT	Use of multiple groups of antihypertensive drugs, including BBs and MRAs
More frequent "hidden HT" than in the general population	Performance of out-of-office BP measurements, especially in patients with diabetes and elevated BP

*Difference between systolic and diastolic BP

Abbreviations: BBs, beta-blockers; TLDs/TDs, thiazide-like diuretics/thiazide diuretics; HFpEF, heart failure with preserved ejection fraction; MRAs, mineralocorticoid receptor antagonists; HT, hypertension; OSA, obstructive sleep apnea; BP, blood pressure; MS, metabolic syndrome

that SGLT2 inhibitors lower BP by approximately 3.6/1.7 mm Hg at ABPM [155].

Hypertension treatment

Table 11.1 shows the characteristics of HT patients with relation to a continuum of obesity → MS → diabetes → HFpEF. The principles of HT treatment on a continuum of obesity → MS → diabetes → HFpEF are described below (Figure 11.3) [64, 142–145]:

- primary HT treatment is based on a combination of ACEIs/ARBs with TLDs/TDs and/or CCBs;
- as a first step, the combination of ACEIs/ARBs with TLDs/TDs is justified due to the importance of sodium sensitivity and hypervolemia in the development of HT in patients with obesity and MS/diabetes;
- the recommended drug combinations within the "basic three" are equally effective in patients with and without obesity [156];
- indapamide and chlorthalidone are the preferred drugs among diuretics (for eGFR ≥30 ml/min/1.73 m^2, and in the case of chlorthalidone for eGFR <30 ml/min/1.73 m^2), while loop diuretics [should be included for indications such as symptoms of congestion, or the absence of BP control as a fifth antihypertensive drug [157, 158];
- the use of ACEIs/ARBs positively influences glucose metabolism and reduces the risk of developing new cases of diabetes [159];
- in patients with diabetes over 55 years of age, and other cardiovascular risk factors, ACEIs should be considered in order to reduce cardiovascular risk regardless of BP [153]. A higher BMI is linked to greater benefits from using these drugs [160];
- if basic antihypertensive drugs are ineffective, the addition of MRAs may be considered not only because of the cardio- and nephroprotective effects described below but also because their antihypertensive efficacy is higher the greater the waist circumference [161–163];
- when indicated, BBs are recommended for the control of excessive sympathetic nervous system activity, especially nebivolol, carvedilol or bisoprolol, due to their metabolic profile [64]. This is beneficial for patients with increased resting heart rate, which is common in obese or diabetic patients [142]. The use of BBs in patients with HFpEF is under discussion; their effect on exercise tolerance should be assessed during use [164–166].

Treatment of lipid disorders

Pharmacotherapy of lipid disorders in patients on a continuum of obesity → MS → diabetes → HFpEF is based on the following principles [64, 167, 168]:

- the use of potent statins (atorvastatin, rosuvastatin) at the highest tolerated dose to achieve the target serum LDL cholesterol concentration set for the specific risk level;
- if targets are not achieved at the maximum tolerated statin dose, then a combination with ezetimibe is recommended;
- in primary prevention, if the goal of lowering serum LDL cholesterol levels is not achieved despite the maximum tolerated dose of statin and ezetimibe, a combination with a proprotein convertase subtilisin/kexin 9 (PCSK9) inhibitor may be considered;
- in secondary prevention, if the goal of lowering serum LDL cholesterol is not achieved despite the maximum tolerated dose of statin and ezetimibe, a combination with a PCSK9 inhibitor (available under B.101 treatment program) or bempedoic acid is recommended; inclisiran is also available under B.101 treatment program;
- once target serum LDL cholesterol levels have been achieved, target non-HDL cholesterol levels may be considered (Figure 11.2);
- in patients with serum triglyceride levels of 2.3 mmol/l (200 mg/dl) or more despite treatment with statins, the use of omega-3 fatty acids (polyunsaturated fatty acids [PUFAs] at a dose of 2–4 g/day) in combination with

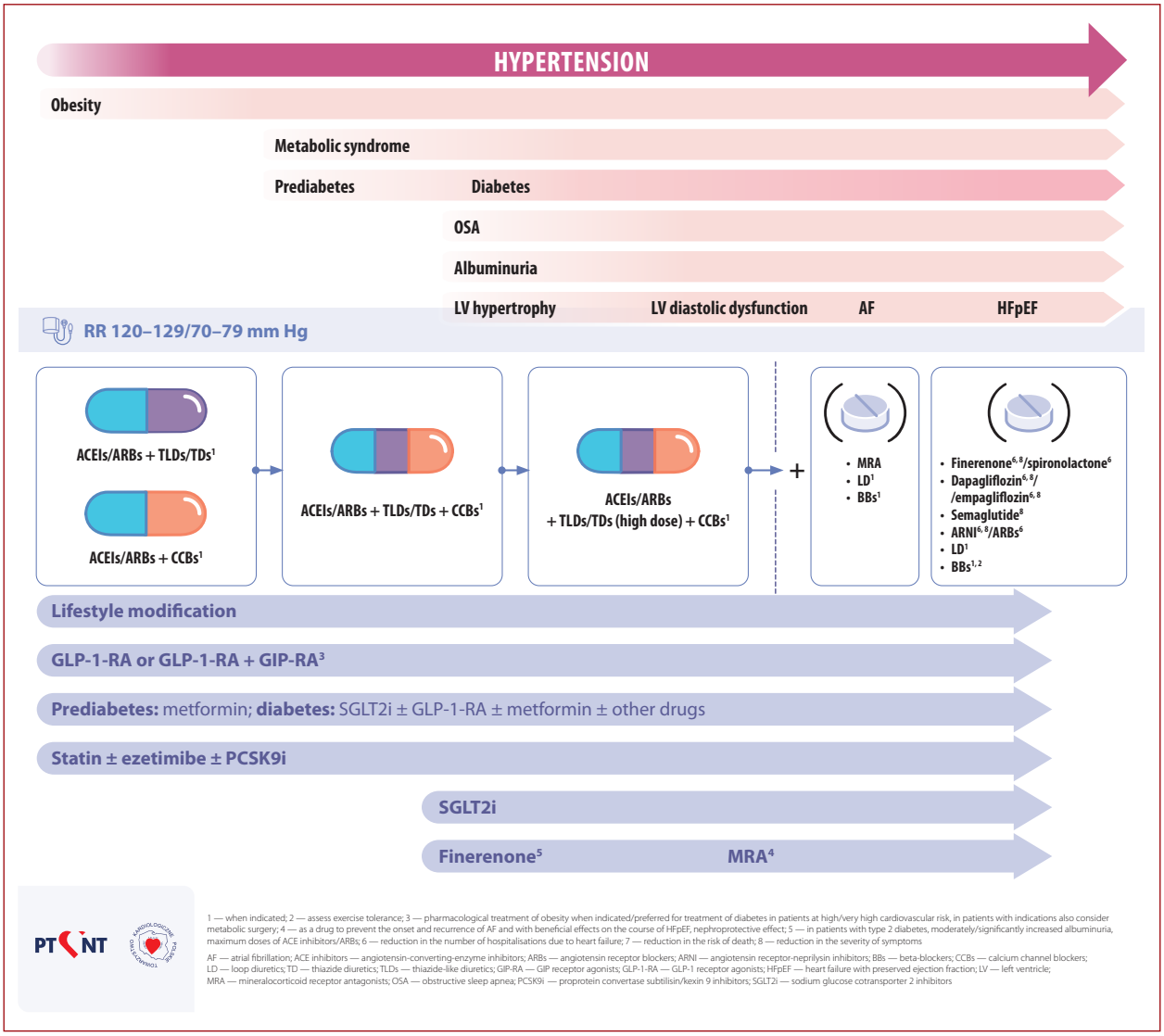


Figure 11.3. Treatment of hypertension (HT) and comorbid conditions on the continuum of obesity → metabolic syndrome → diabetes → HFpEF

a statin may be considered; the use of omega-3 fatty acids at doses of 2 g and above is associated with a higher AF risk;

- in primary prevention in patients who have reached their target serum LDL cholesterol levels with persistent serum triglyceride levels >2.3 mmol/l (>200 mg/dl), fenofibrate in combination with statins may be considered, particularly in patients with low HDL;
- in high-risk patients who have reached their target serum LDL cholesterol levels with persistent serum triglyceride levels >2.3 mmol/l (>200 mg/dl), fenofibrate in combination with statins should be considered, particularly in patients with low HDL.

Additional drugs in the continuum of obesity → MS → diabetes → HFpEF with cardio- and nephroprotective effects

As shown in Figure 11.3, the use of SGLT2 inhibitors, GLP-1 receptor agonists, and MRAs plays an important role in the obesity → MS → diabetes → HFpEF continuum.

The use of SGLT2 inhibitors carries important cardioprotective benefits. In addition, they are well-established in the treatment of HFpEF, where they lower the risk of hospitalisation for HF. These benefits include reduction of left atrial volume and left ventricular mass, improved left ventricular diastolic function, reduced AF risk, a significant decrease in NT-proBNP levels and reduced risk of major ventricular arrhythmias, cardiac arrest and sudden death in patients with HT [169–176].

In patients with CKD, SGLT2 inhibitors further reduce the risk of a composite endpoint, including a 50% or greater reduction in eGFR, development of end-stage renal failure and death from renal causes [177, 178]. In addition, they reduce albuminuria, regardless of glycemic status, eGFR level or baseline severity of albuminuria [179].

There is also increasing evidence supporting the cardioprotective and nephroprotective benefits of GLP-1 re-

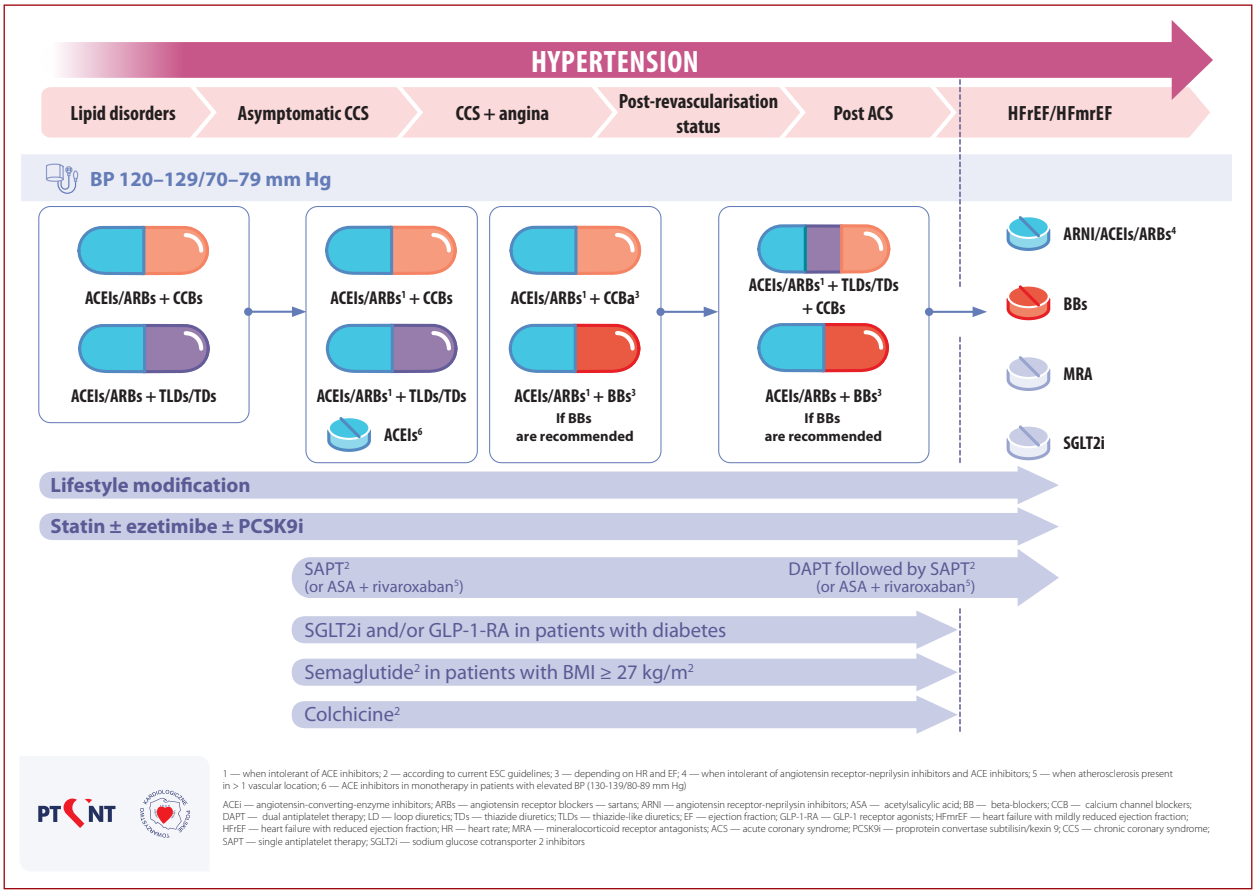


Figure 11.4. Treatment of hypertension (HT) in the continuum of atherosclerotic cardiovascular disease

ceptor agonists [180]. In studies involving patients with HFpEF and obesity, semaglutide significantly reduced the severity of HFpEF symptoms according to the Kansas City Cardiomyopathy Questionnaire — The Clinical Summary Score (KCCQ-CCS), increased the distance in the 6-minute walk test and had a beneficial effect on echocardiographic parameters, including a reduction in left atrial volume [140, 141, 181].

Mineralocorticoid receptor antagonists are also an important component of therapy in the obesity → metabolic syndrome → diabetes → HFpEF continuum. In the FINEARTS-HF trial, finerenone demonstrated the ability to reduce the risk of hospitalisation for HF in patients with HFpEF and a composite endpoint including deaths and hospitalisations. Previous studies indicate that MRAs reduce albuminuria and inhibit the progression of CKD in patients with diabetes and CKD (finerenone), reduce the frequency of AF attacks, reduce left ventricular hypertrophy and inhibit myocardial fibrosis [161, 180, 182–186].

11.3. The "cardiac" patient with HT and a continuum of atherosclerotic cardiovascular disease

The change in approach to coronary artery disease through the concept of chronic coronary syndromes (CCS) allows a holistic view of atherosclerosis-induced cardiovascular disease. This process starts with atherosclerosis risk factors, leads to subclinical coronary atherosclerosis, CCS with angina, acute coronary syndrome (ACS) and ends with heart failure with reduced ejection fraction (HFrEF) (Figure 11.4) [5, 148, 188].

Management of HT in patients on the continuum of cardiovascular disease secondary to atherosclerosis

- Therapy aims to lower the systolic BP to 120–129 mm Hg, provided the patient tolerates the treatment well [5, 148].
- In patients with CCS, ACEIs (or ARBs, if intolerant) are recommended, especially in cases of coexisting HT, diabetes or HF [5, 148].
- ACEIs should be considered in CCS patients at very high risk of cardiovascular events regardless of BP [5, 148].
- Antihypertensive treatment should be initiated at BP of 130–139/80–89 mm Hg (ACEI monotherapy) or combination therapy for HT [5, 148].
- In HT therapy, one should stick to the basic algorithm, using the "basic three" drugs [5, 148]. The combination of ACEIs and CCBs (using SPCs) is preferred. If there is an indication for BBs, the combination of ACEIs and BBs (using SPCs) may be considered [5, 148, 189].
- Patients with CCS and angina may benefit from CCBs and BBs [5, 148].

- Patients with HFrEF should be treated with angiotensin receptor-neprilysin inhibitors ARNIs) or ACEIs (or ARBs, if intolerant), BBs, MRAs and SGLT2 inhibitors [5, 148].

Other drugs reducing cardiovascular risk in patients with CCS

- Potent statins (atorvastatin, rosuvastatin) are recommended to achieve LDL cholesterol targets. If statins alone are insufficient, then ezetimibe is included. If targets are still not met, then bempedoic acid or a PCSK9 inhibitor (available under the B.101 programme) is considered. Inclisiran is also available under the B.101 programme [148].
- Antiplatelet therapy (single or dual), anticoagulant therapy and their combination (including acetylsalicylic acid (ASA) with low-dose rivaroxaban), is used according to the ESC guidelines [148, 190].
- In patients with type 2 diabetes, SGLT2 inhibitors and/or GLP-1 receptor agonists are recommended, irrespective of baseline or target glycated hemoglobin (HbA1c) levels and antihyperglycemic drugs used [148].
- Low-dose colchicine (0.5 mg daily) can be considered in patients with atherosclerotic coronary artery disease [148].
- Semaglutide can be considered in overweight (BMI >27 kg/m^2) or obese patients, even without diabetes, to reduce cardiovascular risk [148].

11.4. Hypertension in patients with a history of stroke

Hypertension is a key and modifiable risk factor for vascular damage to the central nervous system. The association of HT with stroke risk is stronger than for other complications such as ischemic heart disease [191, 192]. Observational studies have shown an almost linear relationship between BP values and its variability and the risk of ischemic stroke, intracerebral hemorrhage and vascular dementia [191–194]. HT is estimated to cause at least 45% of ischemic strokes and 74% of primary intracerebral hemorrhages [191, 192]. Diabetes and HT sequelae such as AF and heart failure (HFpEF and HFrEF) further increase the risk of stroke in patients with HT [195, 196].

In the context of long-term stroke prevention, several placebo-controlled studies have shown that HT pharmacotherapy is effective in reducing the risk of first and subsequent acute cerebrovascular events, regardless of the drugs used [58, 197–200]. Fewer data are available for dementia risk reduction [201, 202].

Patients who benefit more from antihypertensive therapy in terms of stroke risk are those who:

- achieve a greater reduction in BP;
- experience less BP variability;
- use diuretics (especially TLDs), CCBs and ARBs/ACEIs;
- use combination therapy rather than monotherapy [58, 197, 199, 203–211].

Principles of hypertension therapy

- Available data from randomized trials and data from observational studies suggest that in patients with HT after TIA (transient ischemic attack) or after ischemic stroke, the target BP should be similar to that recommended for people with HT [212, 213]. In chronic BP control in patients after TIA, ischemic stroke and cerebral hemorrhagic stroke, a target of less than 130/80 mm Hg, but not less than 120/65 mm Hg is aimed for, provided good clinical tolerance [211] [214–216]. The exception is patients with symptomatic intracranial artery stenosis, in whom it is recommended to achieve values below 140/90 mm Hg [217]. Antihypertensive treatment is initiated immediately after a TIA incident and after the onset of intracerebral hemorrhage, whereas in patients after ischemic stroke, it is deferred for a few days after clinical stabilisation has been achieved [218, 219].
- In patients without established HT prior to an episode of TIA/cerebral ischemic stroke, in whom values ≥130/80 mm Hg are maintained in office measurements after the above-mentioned episode, antihypertensive treatment may be beneficial in terms of reducing recurrent vascular episodes. Target systolic BP values are in the range of 120–129 mm Hg, subject to good tolerance [5, 214, 215, 220].
- Therapy should be individualized, taking into account the patient's degree of functionality and the effect of reduced BP on daily functioning [221].
- It is advisable to monitor BP outside the office (e.g. BP at night, BP after meals) and verify the readings with an orthostatic test, especially in patients who function independently.
- The findings of new randomized trials in stroke patients are awaited [222], but extrapolated evidence suggests that SPC-based pharmacotherapy from the start of treatment is more effective in reducing cardiovascular risk (including stroke risk) than using several separate tablets [223].
- The greatest benefit in secondary prevention comes from a strategy based on controlling HT and all other risk factors associated with cerebrovascular disease.

11.5. Hypertension in patients with peripheral artery disease

Antihypertensive therapy in patients with peripheral artery disease (PAD) should holistically consider other cardiovascular diseases, treating HT as a concomitant disease. It is crucial to minimise the use of symptomatically acting drugs that do not affect the patient's life expectancy and overall morbidity. A patient with PAD should have BP measured in both arms at each visit. In patients with lower extremity arterial disease (LEAD), it is also important to determine the AHI. Because of the risk of atherosclerotic changes in the small vessels, including the retinal microcirculation, patients with LEAD should have an ABPM performed once a year to assess the degree of BP control and diurnal profile.

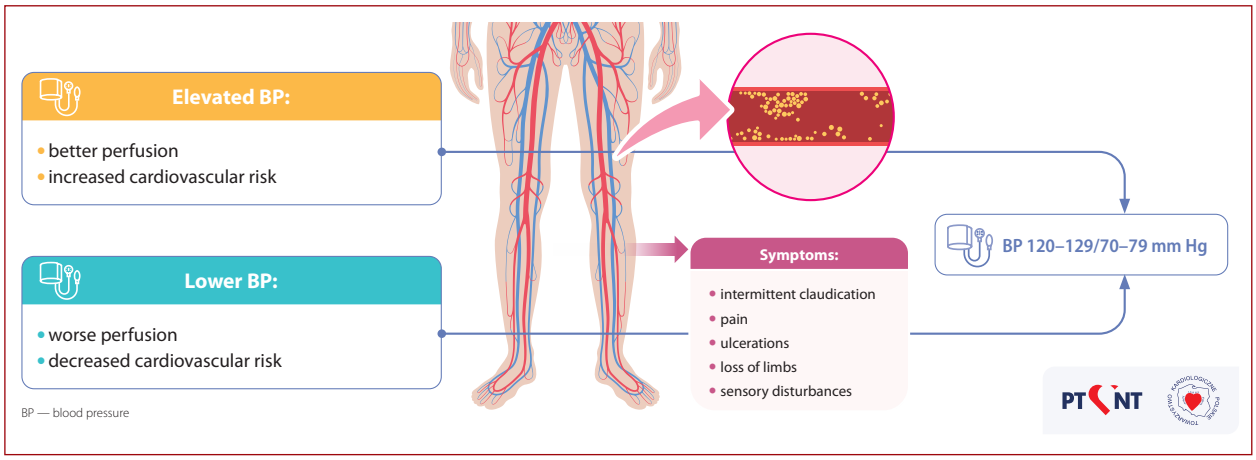


Figure 11.5. Blood pressure (BP) and the risk of worsening limb perfusion and increasing cardiovascular risk. Based on [224, 225]

This is especially important in those with glaucoma (risk of excessive night-time BP drops).

Treatment of HT with coexisting PAD raises concerns of worsening ischemia and increasing the risk of stroke or amputation. However, therapy strives to balance the benefits of BP control and not exacerbate ischemia (Figure 11.5). Effective antihypertensive therapy significantly reduces the long-term risk of cardiovascular events [224–226]. With good tolerance, lowering BP to 120–129/70–79 mm Hg is recommended in most patients [225]. The principles of pharmacotherapy are similar to those used in uncomplicated HT [4].

Myths about the risk of deterioration of limb blood supply by BBs need to be dispelled [227]. Meta-analyses indicate that these drugs do not worsen the symptoms of intermittent claudication or increase the risk of ischemia. On the contrary, BBs may improve prognosis, especially in patients with HFrEF. BBs can be safely used for HT coexisting with LEAD and specific indications. The guideline emphasises that especially those with vasodilatory effects may prolong the distance in the intermittent claudication and improve the clinical condition of the patient [228, 229].

11.6. Hypertension in patients with chronic kidney disease

Hypertension is a key risk factor for the development and progression of CKD. Effective treatment of HT and achievement of target BP slow the progression of CKD and reduce cardiovascular risk. HT and nephroprotective treatment in patients with CKD should start immediately after diagnosis. SGLT2 inhibitors have a strong nephroprotective effect, especially in patients with moderately/significantly increased albuminuria. They also have, as described above, a weak antihypertensive effect [230, 231].

Nephroprotective treatment should be implemented in CKD patients with elevated BP (Figure 11.6) [230, 231]. If BP remains elevated, additional antihypertensive drugs should be considered in addition to the ACEIs/ARBs used, especially with an ACR ≥30 mg/g [4, 5, 48]. Target BP in patients with CKD is controversial and varies in guidelines [4, 5, 48]. Generally, it should be 120–129/70–79 mm Hg with regular control of serum creatinine, avoiding too-low BP [4, 5]. SPRINT and ESPRIT trials, for instance, have shown that intensive BP control was associated with increased rates of acute kidney injury (SPRINT) and renal events (ESPRIT) but reduced the risk of death and cardiovascular events [75, 76].

Principles of HT therapy (Figure 11.6)

- Combination of ACEIs/ARBs with CCBs and/or TLDs/TDs using SPCs [4, 5].
- In patients with albuminuria >30 mg/g, ACEIs/ARBs should be used at the maximum tolerated dose [4, 5, 48].
- The choice of diuretic should depend on the eGFR.
  - — therapy is based on TLDs/TDs for an eGFR ≥30 ml/min/1.73 m^2, and loop diuretics should be included in the absence of BP control or other indications;
  - — therapy is based on chlortalidone for eGFR <30 ml/min/1.73 m^2, and loop diuretics should be included in the absence of BP control or other indications. When loop diuretics are concerned, torasemide is recommended due to its longer duration of action and better tolerability profile than furosemide [4, 5, 157].
- It is common for patients with CKD to have elevated BP at night and without its decrease during sleep. This may be due to inadequate treatment with diuretics. Depending on the eGFR (see above), treatment with TLDs/TDs or loop diuretics, as well as spironolactone, should be intensified [4, 5, 48, 114, 157].
- Finerenone is used as a nephroprotective drug in CKD patients with type 2 diabetes mellitus and an eGFR ≥25 ml/min/1.73 m^2 who have persistent albuminuria ≥30 mg/g despite full-dose ARBs or ACEIs and are not prone to hyperkalemia. It has a significant (but lower than spironolactone) risk of hyperkalemia and an moderate (lower in office measurements, higher in ABPM) reduction in BP. In patients with an eGFR

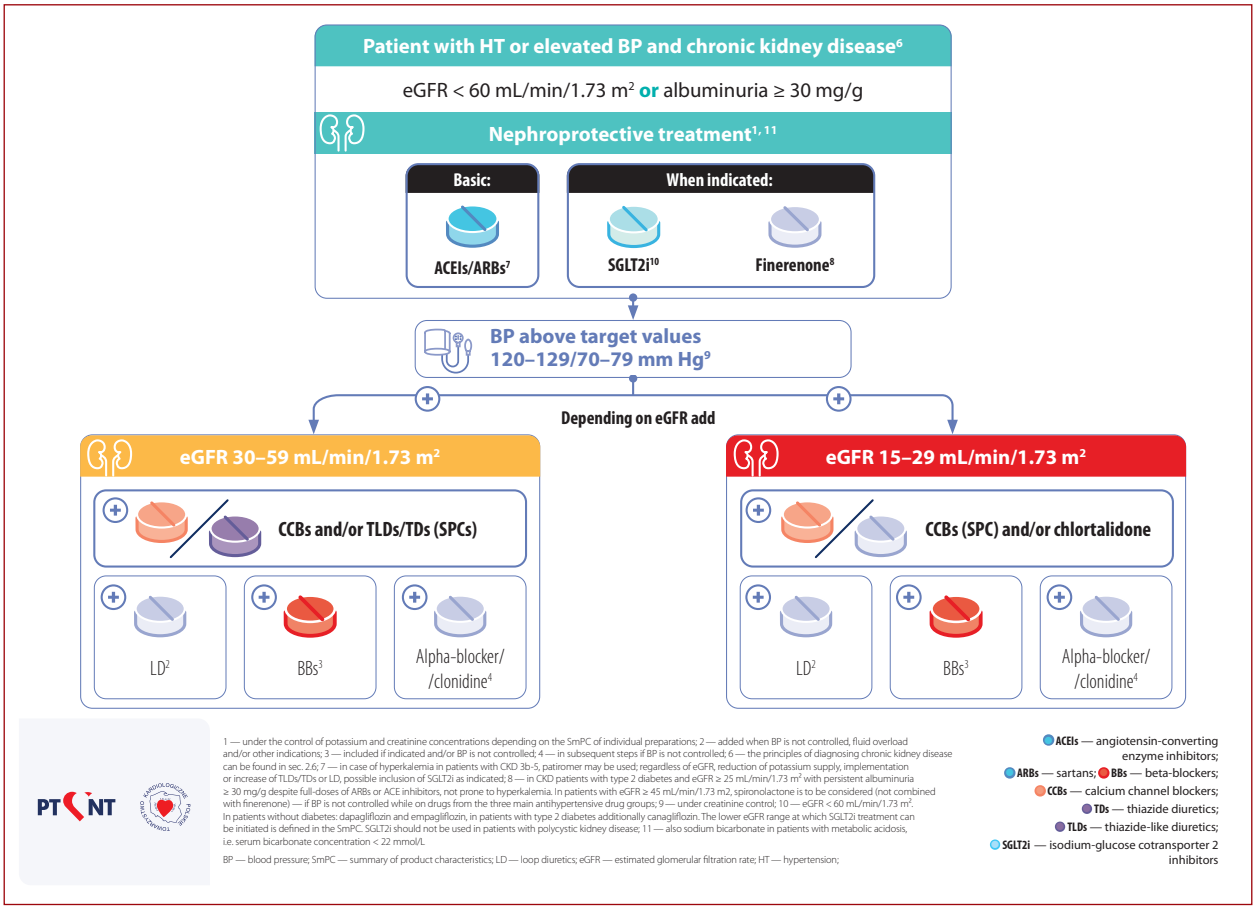


Figure 11.6. Management of patients with hypertension (HT) and chronic kidney disease. Developed based on [4, 5, 48]

≥45 ml/min/1.73 m², in whom the basic three antihypertensive drugs are ineffective, the addition of spironolactone is recommended because of its proteinuria-reducing effect and more pronounced antihypertensive effect. In patients with an eGFR below 45 ml/min/1.73 m² or a potassium concentration of more than 4.5 mmol/l, spironolactone should be used with caution due to the risk of hyperkalemia. Spironolactone should not be combined with finerenone [4, 5, 48, 232, 233].

When to discontinue ACEIs/ARBs in patients with CKD?

ACEI/ARB discontinuation increases cardiovascular and renal risk and should be avoided [234]. Inclusion of these drugs can lower the eGFR by 10%–15%. If the decrease exceeds 30%, then withdrawal should be considered, and renal artery stenosis or other causes should be ruled out [4]. For hyperkalemia in patients with an eGFR <45 ml/min/1.73 m², potassium-binding drugs such as patiromer, available in Poland, may be considered, preventing the need to discontinue ACEIs/ARBs [235]. Regardless of the eGFR, one should try to reduce dietary potassium supply, use or increase doses of TLDs/TDs or loop diuretics, and consider including SGLT2 inhibitors as indicated.

11.7. Hypertension in patients with atrial fibrillation

Patients with HT are almost twice as likely to develop AF as those with normal BP [236, 237]. Regular screening for AF in patients with HT is therefore recommended [238]. In patients with paroxysmal AF and HT, optimal pressure control is crucial, reducing the risk of recurrent AF and cardiovascular events [238–240]. Studies indicate that patients with AF whose BP is adequately controlled are less likely to experience strokes [241, 242]. Target BP in patients with HT and AF is 120–129/70–80 mm Hg [243, 244].

Appropriate pharmacological treatment of HT and HF can prevent AF. It works by limiting atrial stretch, and drugs that inhibit the renin–angiotensin system may further protect against electrical and structural remodelling of the heart. As an outcome and marker of atrial remodelling, AF is closely associated with atrial cardiomyopathy. Drugs affecting atrial remodelling may prevent new episodes of AF and act as unconventional antiarrhythmics [238].

ACEIs or ARBs are preferred in the treatment of patients with AF and HT, but MRAs should also be considered. Effective combinations of ACEIs/ARBs with CCBs or TLDs/TDs are recommended for optimal BP control. Beta-blockers are recommended to control HR [238]. In patients with HT and AF, anticoagulant treatment is necessary for the prevention of ischemic stroke. HT increases both the risk

of stroke and the risk of hemorrhagic complications. HT is not a contraindication to anticoagulant treatment, whereas poor BP control increases the risk of hemorrhages.

11.8. Gestational hypertension

Hypertensive disorders of pregnancy include [4, 131]:

- **pre-existing** (chronic) HT: diagnosed before pregnancy or up to the 20th week of gestation;
- **gestational HT**: developing after the 20th week of gestation; it often resolves within six weeks postpartum. It is not accompanied by proteinuria or biochemical abnormalities;
- **PE**;
- **eclampsia**;
- **HELLP** (hemolysis, elevated liver enzymes, low platelets) syndrome: characterized by clotting abnormalities, liver damage and thrombocytopenia.

If women with pre-existing HT after the 20th week of gestation experience an exacerbation of HT and develop symptoms typical of pre-eclampsia, such as proteinuria or significant organ dysfunction, a diagnosis of HT with superimposed pre-eclampsia is made [4, 131].

The cut-offs values for diagnosing HT in pregnant women are the same as in the general population: ≥140/90 mm Hg, confirmed by out-of-office measurements within seven days in the first trimester and up to three days in the second and third trimesters [4, 131].

Antihypertensive drugs and the prevention of AF

- Studies in which AF was an additional endpoint suggest that ACEIs and ARBs may prevent the first occurrence of AF in patients with left ventricular dysfunction, LVH or HT. ACEIs and ARBs are beneficial as first-line drugs in patients with AF; however, ARBs do not reduce AF severity in patients without structural heart disease [238].
- Recent studies using Mendelian randomisation indicate that BBs are as effective as other classes of antihypertensive drugs [245].
- Aldosterone plays a role in the induction and perpetuation of AF, and the use of MRAs reduces the burden of AF. Meta-analyses have shown that MRAs significantly reduce the incidence of first occurrence and recurrence of AF, although they do not reduce the risk of postoperative AF. In contrast, MRAs reduce the incidence of AF in both HFrEF and HFpEF patients [183, 236, 237, 246, 247].

Gestational hypertension

Management of gestational HT includes [4, 131, 248, 249]:

- maintaining a normal diet without significant salt restriction. Women with chronic HT should continue a low-sodium diet;
- physical activity: at least 140 minutes of moderate exercise per week (30–60 min, 3–4 times per week).
- pharmacological treatment of HT is initiated when BP is ≥140/90 mm Hg (according to the principles shown in Figure 11.7).
- maintaining BP during therapy in the range of 110––140/80–85 mm Hg;
- ASA at a dose of 150 mg daily administered in the evening, started by the 16th week of gestation to prevent pre-eclampsia;
- in case of BP ≥160/110 mm Hg or symptoms indicative of pre-eclampsia, hospitalisation is indicated.

Pre-eclampsia

Pre-eclampsia develops after the 20th week of gestation in women with previously normal BP or exacerbates pre-existing HT; it is accompanied by proteinuria and/or a risk to fetal or maternal well-being. It rarely develops in the puerperium. It is caused by increased vascular resistance, platelet propensity to aggregate, activation of the coagulation system, impaired endothelial function, and placental abnormalities. Risk factors are shown in Table 11.2 [4, 131, 248].

In women at high risk of PE, ASA at 150 mg daily, started by the 16th week of gestation, and moderate physical activity are recommended as prophylaxis. Women with a history of gestational HT or PE have an increased risk of HT, HF, cardiovascular events and premature death. They should be regularly assessed for risk factors, and intensive treatment should be instituted if they develop [4, 131, 248].

11.9. Hypertension in young adults

Diagnosis of HT at a young age increases the risk of death and accelerates the occurrence of HMOD. High BP in young adults often persists also in later years of life, which is known as "tracking". This phenomenon is associated with an unfavourable prognosis in both short and medium-term follow-up and increases the risk of cardiovascular events [250].

Selected patients should be referred to specialist centres for detailed assessment for secondary causes of HT. In young adults, it is worth considering early introduction of pharmacological treatment alongside lifestyle modifications. Patient education and close collaboration between GPs, hypertensiologists, cardiologists and the patients are crucial. This integration of efforts increases the effectiveness of HT diagnosis and therapy in young adults.

Recent studies indicate that ISH is most common in older adolescents and young adults with primary HT. This type is diagnosed in 66% of patients, mainly among boys and men. Systolic-diastolic HT was found in 30% of patients and isolated diastolic HT in 4% [251]. Among young adults aged 18 to 40 (mean 25 years), ISH predominates in men. Women are more commonly affected by systolic-diastolic HT or isolated diastolic HT [252].

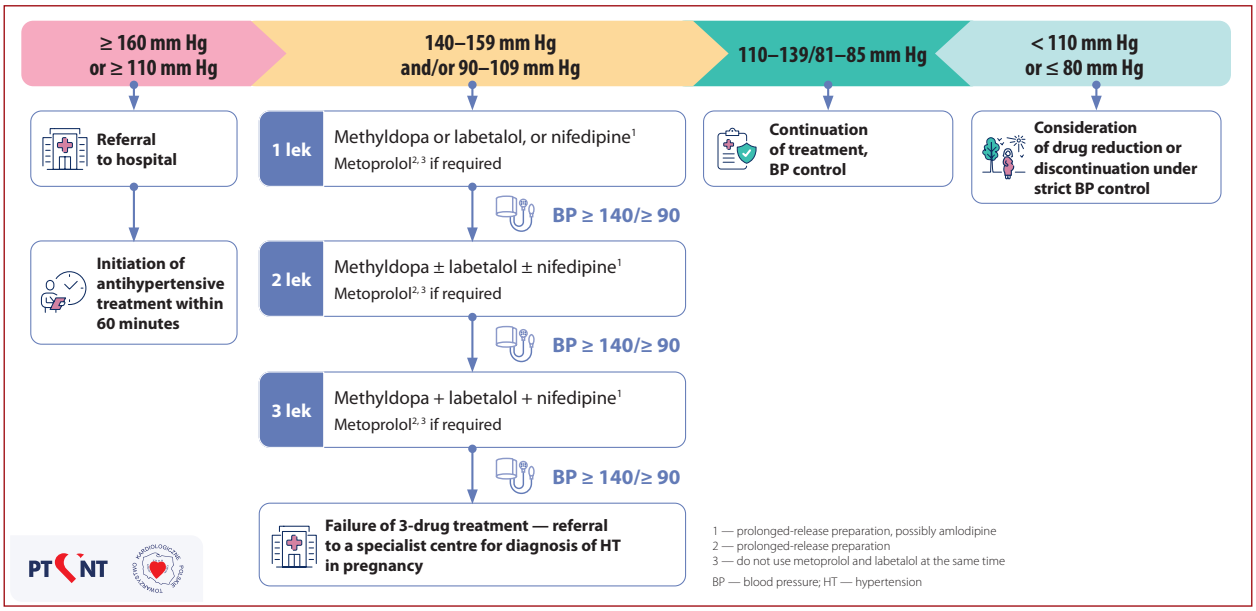


Figure 11.7. Treatment of gestational hypertension (HT). Based on [131]

Table 11.2. Risk factors for pre-eclampsia (PE) [4, 131, 248]

Intermediate risk	High risk
First pregnancy	History of gestational HT
Age >40 years	Chronic kidney disease
In between pregnancy interval >10 years	Systemic lupus
Pre-pregnancy BMI of >35 kg/m^2	Antiphospholipid syndrome
History of PE in the patient's mother	Type 1 or type 2 diabetes
Multiple pregnancy	Chronic HT

Abbreviations: BMI, body mass index; HT, hypertension

Isolated systolic HT in young people is a complex phenomenon. In some, particularly tall and physically active men, it may result from pulse pressure amplification. Despite a normal central BP in the aorta, it may reflect an extreme physiology, called pseudohypertension. This type of HT is also sometimes the result of increased cardiac output with not yet increased peripheral resistance (hyperkinetic circulation).

The management of young people with ISH follows the following principles:

- treatment should be based on the general principles of HT management;
- non-invasive measurement of central BP may be valuable, although it is rarely available and not mandatory;
- for ISH patients with systolic BP values between 140 and 159 mm Hg and no HMOD or cardiovascular risk factors, non-pharmacological treatment for 6–12 months is recommended;
- for ISH with systolic BP values ≥160 mm Hg or with coexisting HMOD or cardiovascular risk factors, initiation of pharmacotherapy is indicated.

11.10. Hypertension in cancer patients

Hypertension is the most common comorbidity in cancer patients. Unhealthy diet, obesity, physical inactivity, smoking and alcohol consumption are common risk factors that contribute to the prevalence of HT in this group. In cancer patients, HT, like other cardiovascular risk factors and recognized cardiovascular disease, increases the risk of cardiotoxicity of anticancer treatment (Figure 11.8).

Increases in BP during the use of VEGF pathway inhibitors

- BP rise occurs within hours or days. It is dose-dependent and usually resolves when treatment is stopped. With small-molecule TKIs, such as sorafenib and sunitinib, this happens within a few days. With antibodies such as bevacizumab, it may take several weeks.
- The risk of elevated BP is increased in patients with existing HT or cardiovascular diseases. It is higher in patients previously treated with anthracyclines, at advanced age, who are smokers, or have hyperlipidemia or obesity.
- BP usually decreases after completion of VEGF inhibitor therapy. The dose of antihypertensive drugs should then be reduced accordingly or treatment discontinued.

Hypertension may develop or worsen due to malignancy (stress, pain) or treatment such as vascular endothelial growth factor receptor (VEGF) inhibitors, second- and third-generation BCR-ABL tyrosine kinase inhibitors (TKIs), brigatinib, ibrutinib, fluoropyrimidines, cisplatin, abiraterone, bicalutamide, enzalutamide and non-cancer therapies such as corticosteroids and non-steroidal anti-inflammatory drugs (NSAIDs) [253].

The management of HT in cancer patients should follow standard principles for other patient groups. It is important

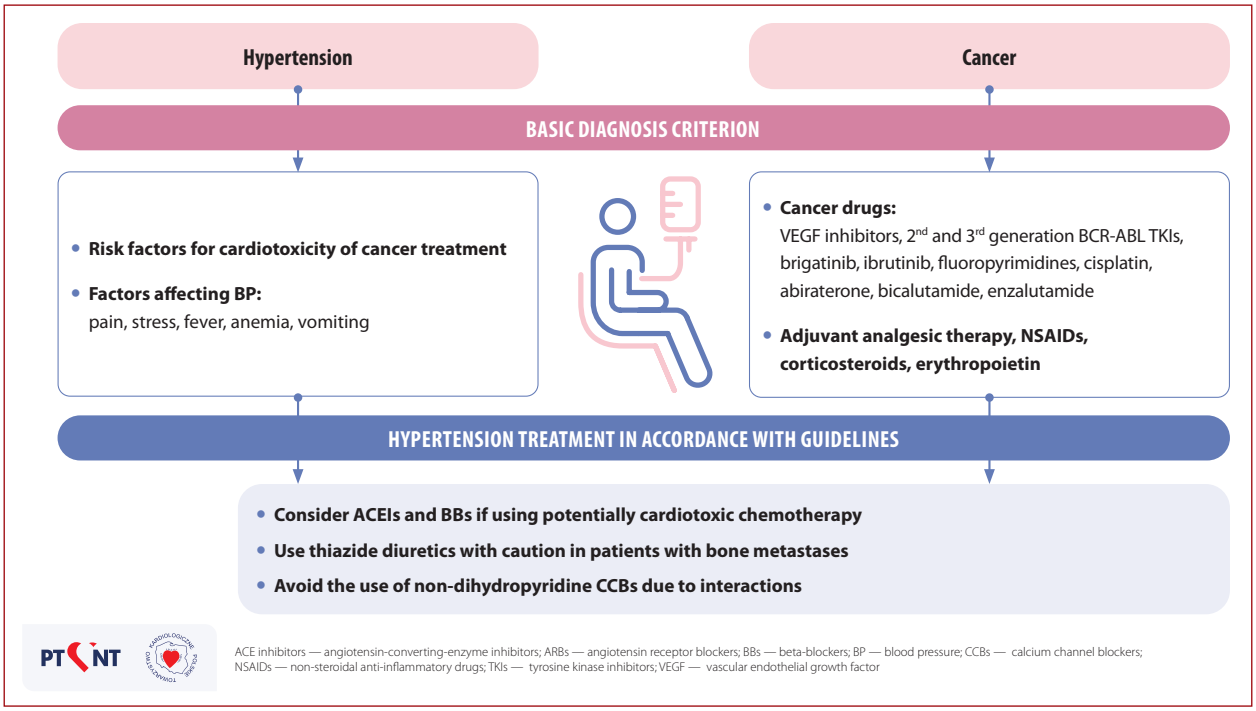


Figure 11.8. Management of hypertension (HT) in cancer patients

to optimise BP control before starting cancer treatment and to monitor it closely. The choice of treatment should take into account the type of cancer treatment and the risk of drug interactions.

Drugs from the ACEI/ARB and CCB groups are preferred. In contrast, TLDs/TDs, which are the mainstay of treatment in the general HT patient population, should be used with caution in this group. In patients with bone metastases, TLDs/TDs may increase the risk of hypercalcemia, and in patients with gastrointestinal symptoms (vomiting, diarrhea) during cancer treatment, TLDs/TDs may exacerbate electrolyte disturbances. In patients treated with androgen synthesis inhibitors or androgen receptor antagonists, MRAs may be effective [253, 254].

Diltiazem and verapamil are not recommended during anticancer treatment as their metabolism is *via* the cytochrome P450 3A4 system, which may lead to interactions with chemotherapeutics and increase drug concentrations in the blood [253].

The inclusion of ACEIs or ARBs and BBs — recommended in HF — should be considered for primary prevention in high-risk patients, especially when targeted drugs are used that may induce heart failure [253].

A distinctive form of HT is observed during treatment with angiogenesis inhibitors, whose main target is the VEGF receptor. When using VEGF inhibitors, close monitoring of BP during the first cycle of treatment is recommended — daily home measurements are preferred. An increase in BP during therapy with these drugs is observed in the majority of patients; antihypertensive treatment often needs to be intensified during cancer treatment and then reduced after the end of the cycle. The aims of monitoring BP values and optimising treatment are to reduce cardiovascular risk and to allow continuation of cancer treatment. The threshold values for withholding cancer treatment are a rise in BP ≥180/110 mm Hg [253].

11.11. Hypertension in elderly patients with frailty and/or multimorbidity

The changing age structure in Western societies, better health and longer life expectancy of the elderly lead to a discussion on the arbitrariness of the definitione of old age. As a result, this position paper refrains from setting specific boundaries for old age [5, 15, 41]. Instead, priority is given to assessing the fitness of patients, regardless of age, in the diagnostic and therapeutic process of HT.

In light of the unequivocal intervention studies that have shown benefits of antihypertensive treatment even after the age of 80, elderly HT patients should be treated similarly to younger patients in decision-making algorithms [206]. This means using the same diagnostic criteria and decision-making BP values for pharmacotherapy. However, in the case of elderly patients, specific conditions that are more common in this age group should be taken into account, such as:

- frailty (in Poland it affects 15.9% of people over 60 years of age) [15];
- multimorbidity, including polypragmasia or short life expectancy [255, 256];
- situational hypotension (orthostatic, postprandial, exercise-induced, nocturnal);
- ISH (affects 26.8% of people over 60 years of age in Poland) [15, 257].

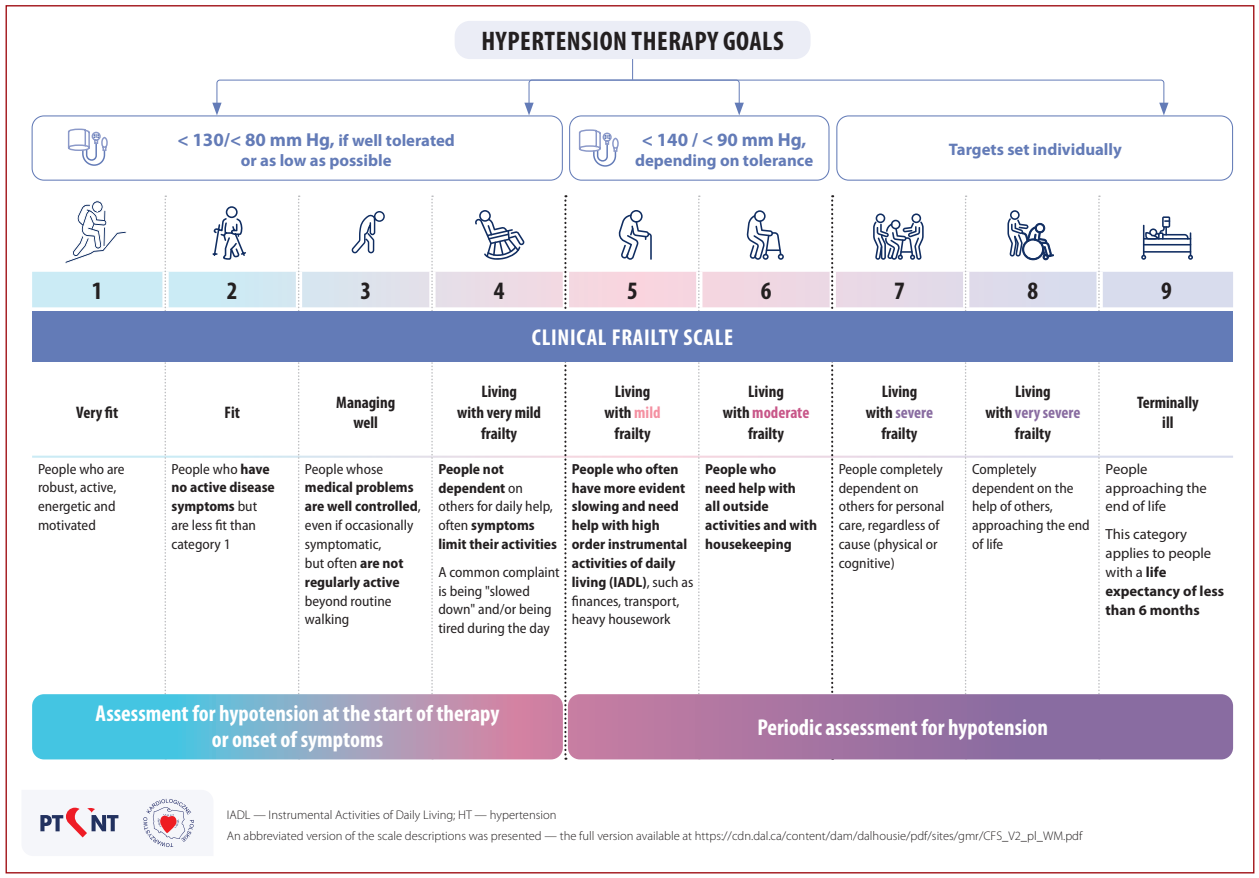


Figure 11.9. Management of hypertension (HT) in elderly patients

Each of these situations requires an individual approach to therapy, which makes it difficult to formulate uniform recommendations. It should also be borne in mind that problems such as frailty or multimorbidity are not just a matter of age and may also be present in people under 60 years of age.

Management in elderly patients

- A key part of the assessment of elderly patients during the diagnosis of HT is a thorough hemodynamic assessment. This includes the risk of orthostatic and postprandial hypotension and excessive BP fall during sleep and after exercise. It is also important to assess the risk of frailty, which is defined as a multidimensional loss of the body's physical, cognitive or social reserves and capabilities [15, 258]. In clinical practice, validated questionnaires are used to assess the presence and severity of frailty, of which the easiest-to-use 9-item scale is recommended (Figure 11.9) [206, 259–262].
- Elderly patients with HT should be provided with a complete set of information on non-pharmacological treatment, which is recommended to be implemented to the maximum extent possible. Recommendations for adequate fluid supply should also be kept in mind.
- Due to the higher risk of polypragmasy in the elderly, with its negative consequences, long-acting drugs administered in an SPC formulation should be preferred in the complex therapy of HT in elderly patients [255]. Exceptions are patients with at least mild frailty, aged ≥80 years, with orthostatic hypotension or a life expectancy of less than 3 years, in whom HT therapy is started with monotherapy.
- The mainstay of antihypertensive therapy in most elderly patients are ACEIs/ARBs in combination with CCBs or low-dose TLDs/TDs (preferentially TLDs). BBs should be considered if indicated, with a preference for SPC preparations. In patients with ISH in whom BBs are not indicated, drugs other than BBs should be considered due to their weaker effect on central BP than other drugs [5].

12. MANAGEMENT OF EMERGENCIES

Emergencies — are characterized by severe HT (≥180/≥110–120 mm Hg) accompanied by acute signs of organ damage (Table 12.1). Such cases are life-threatening and in most patients require immediate intervention (intravenous pharmacotherapy). The key in such circumstances is a rapid lowering of BP with intravenous pharmacotherapy (Figure 12.1) [2, 4, 263].

Typical emergencies:

- **severe HT** in acute conditions: refers to situations requiring urgent BP lowering, such as acute (hemorrhagic

Table 12.1. Emergencies in hypertension (HT) — organ damage. Based on [263]

	Type of organ damage (BARKH)				
	B — brain	**A — arteries**	**R — retina**	**K — kidneys**	**H — heart**
Acute conditions indicative of a hypertensive emergency	a) ischemic stroke b) PRES c) cerebral hemorrhage	a) acute aortic dissection b) pre-eclampsia, HELLP, eclampsia	Keith–Wagener–Barker grade III–IV hypertensive retinopathy	Acute kidney injury Thrombotic microangiopathy	a) acute heart failure b) pulmonary edema c) acute coronary syndrome
Initial BP target	a) when reperfusion treatment (thrombolysis/thrombectomy): lower BP <185/110 mm Hg and maintain within <180/105 mm Hg for at least 24 h • when conservative treatment: gently lower when BP>220/120 mm Hg — ↓ MAP by 15% within 24 h • when coexisting non-cerebral emergency conditions — individual BP targets b) immediately ↓ MAP by 20%–25% c) when spontaneous intracranial hemorrhage of mild to moderate severity and SBP in the range 150–220 mm Hg in the first 6 h, lower SBP <140 mm Hg and maintain in the range 130–150 mm Hg for the following 7 days • in other cases, individual BP targets	a) immediately ↓ SBP <120 mm Hg and HR <60/min b) immediately ↓ SBP <160 mm Hg and DBP <105 mm Hg	SBP <180 mm Hg ↓ MAP by 15%	↓ MAP by 20%–25% over several hours	a) SBP <180 mm Hg or immediate MAP by 25% b) immediately SBP <140 mm Hg c) immediately SBP <140 mm Hg
Treatment	Labetalol, nicardipine, sodium nitroprusside (alternative)	Esmolol (alternatively labetalol/metoprolol) and nitroglycerin or sodium nitroprusside or nicardipine Labetalol or nicardipine, magnesium sulphate, urapidyl when needed		Labetalol, nicardipine, urapidil, sodium nitroprusside (alternative)	Nitroglycerine with a loop diuretic Nitroglycerine or sodium nitroprusside and possibly a loop diuretic Nitroglycerine, labetalol or esmolol; alternatively urapidyl

Abbreviations: BARKH — brain, arteries, retina, kidneys, heart; DBP — diastolic blood pressure; HELLP — hemolysis, elevated liver enzymes, low platelets; HR — heart rate; MAP — mean arterial hypertension; PRES — posterior reversible encephalopathy syndrome; SBP — systolic blood pressure

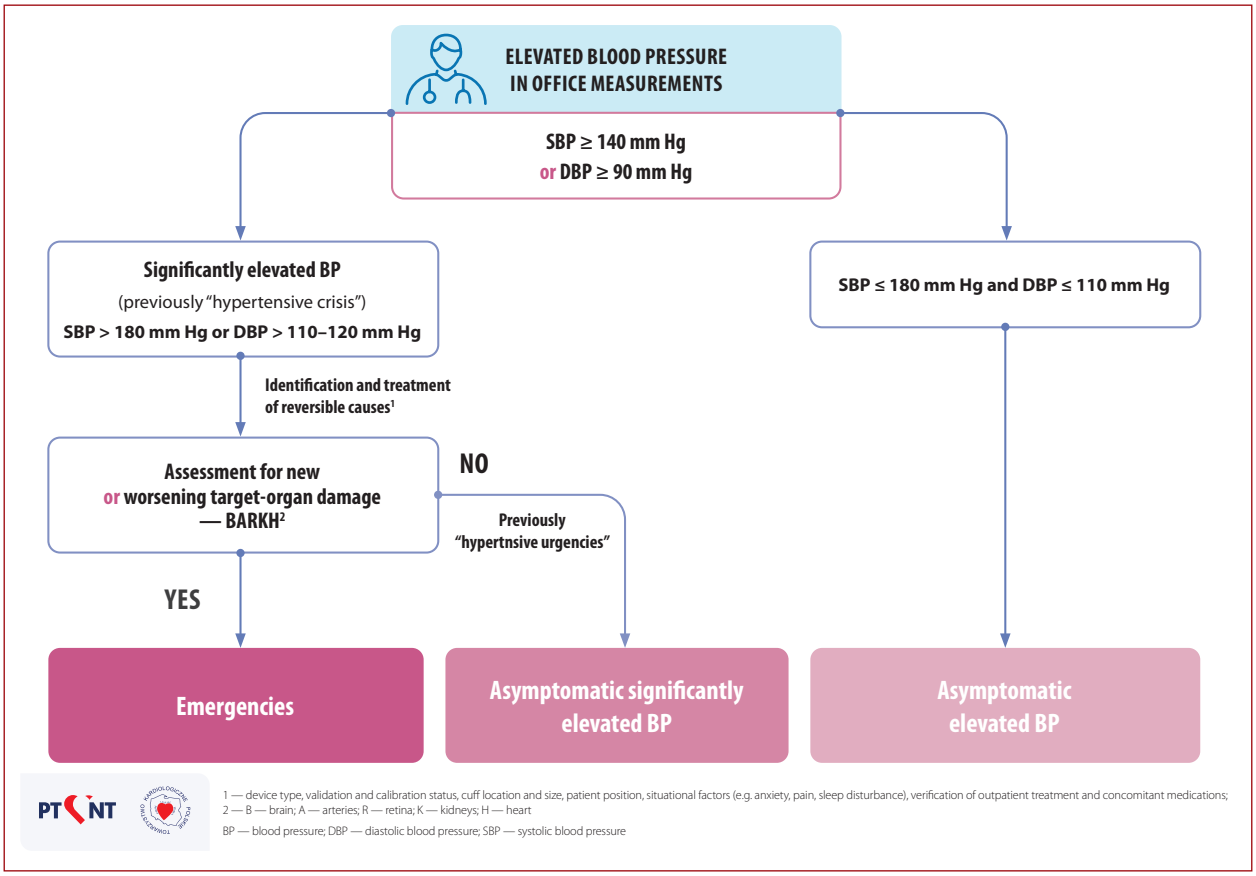


Figure 12.1. Clinical conditions with elevated blood pressure (BP) values in office measurements. Based on [263]

Table 12.2. Diagnosis of emergencies and asymptomatic significantly elevated blood pressure (BP). Based on [4]

Commonly performed tests	Specific examinations
Fundus examination	Troponin, NT-proBNP (suspicion of heart failure and/or acute coronary syndrome)
12-lead ECG	Chest X-ray or ultrasound (lung densities and fluid overload)
Hemoglobin, platelet count, fibrinogen, peripheral blood smear	Echocardiography (heart failure, acute ischemia, aortic dissection)
Creatinine, eGFR, electrolytes, LDH, haptoglobin	CT angiogram of the chest and/or abdomen when aortic disease is suspected (aortic dissection)
ACR, evaluation of urine sediment for red blood cells, leukocytes and/or casts	Brain CT or MR (nervous system involvement)
Pregnancy test in women of childbearing age	Renal ultrasound renal impairment or suspected renal artery stenosis
	Urine sampling for the presence of drugs (cocaine or methamphetamine use)

Abbreviations: eGFR, estimated glomerular filtration rate; ECG, electrocardiogram; LDH, lactate dehydrogenase; MRI, magnetic resonance; NT-proBNP, N-terminal pro-B-type natriuretic peptide; X-ray, radiological/X-ray examination; ACR, albumin/creatinine ratio; CT, computed tomography; ultrasound, ultrasound examination

or ischemic) stroke, aortic aneurysm or dissection, acute HF, ACS and renal failure. In such cases, even a small increase in BP can significantly exacerbate organ failure;

- **HT induced by specific factors**: can be caused by a tumour secreting catecholamines or by exogenous sympathomimetics such as psychoactive substances.
- **severe HT in pregnant women**: includes PE, eclampsia and HELLP syndrome.

The term "**urgent cases**" — currently proposed as **asymptomatic significantly elevated BP** — refers to HT with significantly elevated BP values that are not associated with acute organ damage at the time of the patient's assessment (Figure 12.1).

Malignant HT is a distinct form of emergency in HT characterized by a very poor prognosis when left untreated. It is defined as the coexistence of very high BP and thrombotic microangiopathy and acute renal failure. It is an emergency in which there is fibrinoid necrosis of small arteries and arterioles in the kidneys, retina and brain. Lesions of the fundus, microangiopathy, disseminated intravascular coagulation, encephalopathy or acute heart failure are also possible. Symptoms depend on the organs involved. They may include headaches, visual disturbances, dizziness and other neurological deficits, as well as chest pain and dyspnea. Patients with hypertensive encephalopathy may experience drowsiness, lethargy, tonic-clonic seizures and cortical disorders; blindness may precede loss of consciousness [4, 264]. The management of malignant HT is discussed in detail in a recently published paper [264].

12.1. Management of asymptomatic significantly elevated BP [4, 263]

- Patients generally do not require hospitalisation.
- The range of diagnostic investigations is shown in Table 12.2.
- It is necessary to gradually lower BP with oral antihypertensive drugs, which can be achieved by resuming or intensifying treatment (choice of drugs according to the basic strategy). This process should last 24–48 hours.
- For *ad hoc* BP lowering, short-acting drugs: clonidine, captopril or nitrendipine.
- Significantly elevated BP is one of the most common reasons for presenting to hospital emergency departments. A domestic analysis of these admissions indicates that there is a significant problem of inadequate antihypertensive therapy in this group of patients [265]. The patient should be advised by the treating physician for urgent consultation to modify HT therapy.

12.2. Management of emergencies [4, 263]

- All patients, including pregnant women with BP ≥160/110 mm Hg, should be hospitalized.
- The range of diagnostic investigations is shown in Table 12.2.
- It is important to determine which organs are involved, whether they require specialist intervention beyond lowering BP and to understand the cause of the sudden rise in pressure, which may influence the treatment plan.
- Determine the time scale and extent of BP lowering needed, and select appropriate pharmacological treatment (Table 12.1).
- Use intravenous drugs with a short half-life, which allows fine-tuning of treatment with close monitoring of the patient.
- Oral treatment with ACEIs, ARBs or BBs (with low initial doses and careful escalation) is sometimes effective in malignant HT, as the renin–angiotensin system may be activated by renal ischemia associated with this condition.

13. PERIOPERATIVE TREATMENT OF HT

13.1. Qualification for surgery and preoperative management

The basic recommendations for preoperative management [4, 266] are as follows:

- non-cardiac surgery should be performed when systolic BP is below 180 mm Hg and diastolic BP is below 110 mm Hg.
- surgical treatment should not be postponed in patients with untreated HT whose BP is 140–159/90–99 mm Hg or in those with controlled or almost controlled BP;
- if a patient is untreated and has a BP of at least 160/100 mm Hg, surgery should be postponed until BP control is achieved, unless it is an urgent operation;
- antihypertensive treatment, including BBs, should not be discontinued during the perioperative period. How-

ever, the patient should be monitored for electrolyte disturbances, arrhythmias, bradycardia and hypotension as possible consequences of treatment. BB therapy should not be started in <1 week before surgery;

- ACEIs/ARBs and diuretics can be discontinued on the day of surgery, while SGLT2 inhibitors should be discontinued three days before the planned surgery. Although discontinuation of ACEIs/ARBs on the day of surgery compared with continued therapy has been shown to be associated with fewer episodes of intraoperative hypotension, no differences were found in terms of the incidence of postoperative complications [267].

Changes in BP values may occur during perioperative management. Increases in BP may be induced by induction of anesthesia, intubation, pain associated with surgery and vasopressors, and decreases — by continued anesthesia, volume loss and blood loss.

13.2. Intraoperative management

During surgery, both low and high BP values may increase the risk of complications due to impaired autoregulation of blood flow, especially in older patients. There are no clear guidelines as to the specific BP values that should be maintained during surgery. It is important to try to keep them within a safe range, avoiding large fluctuations, especially episodes of hypotension, and aim for hemodynamic stability [4, 266].

13.3. Postoperative period

In the initial two hours after surgery, it is common to see an elevation in BP values, which usually resolves when antihypertensive treatment is reintroduced. Oral BBs should be restarted as soon as possible. Oral diuretics and ACEIs/ARBs should be restarted within 48 hours, after a thorough assessment of BP and the hydration status of the patient, taking into account the type of surgery performed, i.e. whether it was cardiac or non-cardiac surgery [4, 266].

14. UNCONTROLLED HYPERTENSION

14.1. Definition, characteristics and causes of uncontrolled and resistant HT

Hypertension is considered resistant when, despite the use of three drugs, including a diuretic, in appropriate combinations (ACEIs/ARBs and TLDs/TDs and CCBs) and at maximum tolerated doses, BP values in office measurements remain ≥140/90 mm Hg. Resistant HT defined in this way affects 10%–20% of patients. However, after taking into account ABPM to exclude the white coat effect and adherence to therapeutic recommendations (taking at least 80% of medication doses), the incidence of truly resistant HT is lower at around 5% [2, 4, 5, 268].

The reduction of target BP values to below 130/80 mm Hg means that many patients, although not meeting the definition of resistant HT, have uncontrolled HT. This is an increasingly common clinical problem. Patients with uncontrolled HT, especially those with resistant HT, have a higher incidence of HMOD and a higher cardiovascular risk. This risk also depends on the number of antihypertensive drugs used.

The pathophysiology of resistant HT includes overexpression of vasoconstrictive neurohormonal factors, renal dysfunction with fluid overload and, in the elderly, aortic and large artery stiffness. Common clinical conditions associated with resistant HT include obesity, alcohol abuse, salt-rich diet, CKD and diseases causing secondary HT [2, 4, 268, 269].

14.2. Diagnostic and therapeutic management of patients with suspected resistant HT

Figure 14.1 shows the algorithm for the diagnostic and therapeutic management of patients with suspected resistant HT.

The first step is to verify the appropriate choice of HT pharmacotherapy. The best option is to replace the current treatment with a single pill triple drug combination containing ACEIs/ARBs, TLDs/TDs and CCBs at maximum tolerated doses. This improves BP control in many patients [2, 4, 5, 268].

The second step is to check whether BP is indeed inadequately controlled, by taking home measurements (correctly taken) or ABPM. This helps to rule out the white coat effect, which is the second most common cause of pseudo-resistant HT [270].

The third step: in conversation with the patient, it is also worth verifying compliance with therapeutic recommendations (non-adherence is the most common cause of pseudo-resistant HT), including regular medication and lifestyle changes. Weight reduction, regular physical activity, reduction of salt and alcohol intake are important. A significant antihypertensive effect of intensive implementation of lifestyle modification recommendations has been shown in patients with resistant HT [271, 272]. Common reasons for non-adherence to therapeutic recommendations are: forgetting to take medication, poor motivation due to lack of awareness of the effects of HT, side effects of medication (including so-called multiple drug intolerance), poor tolerance of lower BP values and lack of symptoms at the onset of HT, too many medications used [273, 274]. Improvements in adherence can be achieved by using SPCs [2, 4, 5, 268, 269].

The fourth step: it is important to review the medications and substances taken by the patient, including those taken ad hoc, which may increase BP. These include drugs such as NSAIDs, corticosteroids, pseudoephedrine and combined contraceptives, theophylline, as well as substances such as liquorice and cocaine and other stimulants and dietary supplements.

The fifth step: often carried out already in reference centres, is screening for secondary causes of HT, which often lead to resistant HT. If a secondary form of HT is diagnosed, the key is to treat the underlying disease (Figure 4.5,

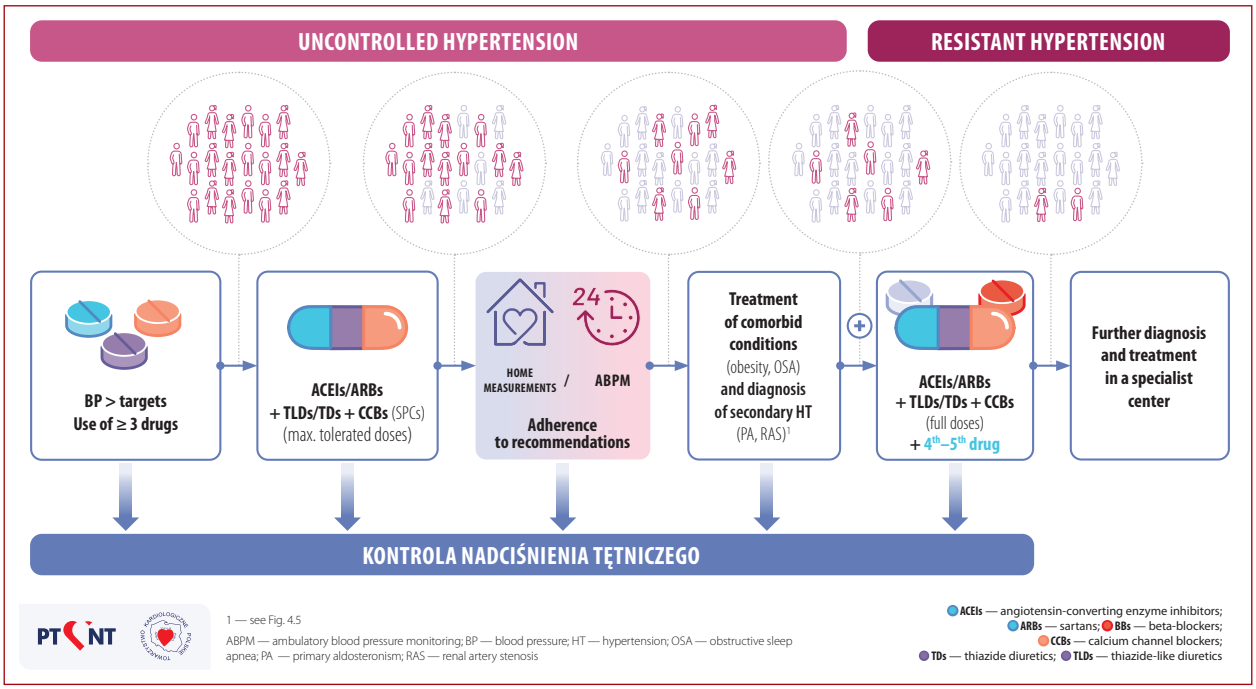


Figure 14.1. Algorithm for the management of patients with suspected resistant hypertension (HT)

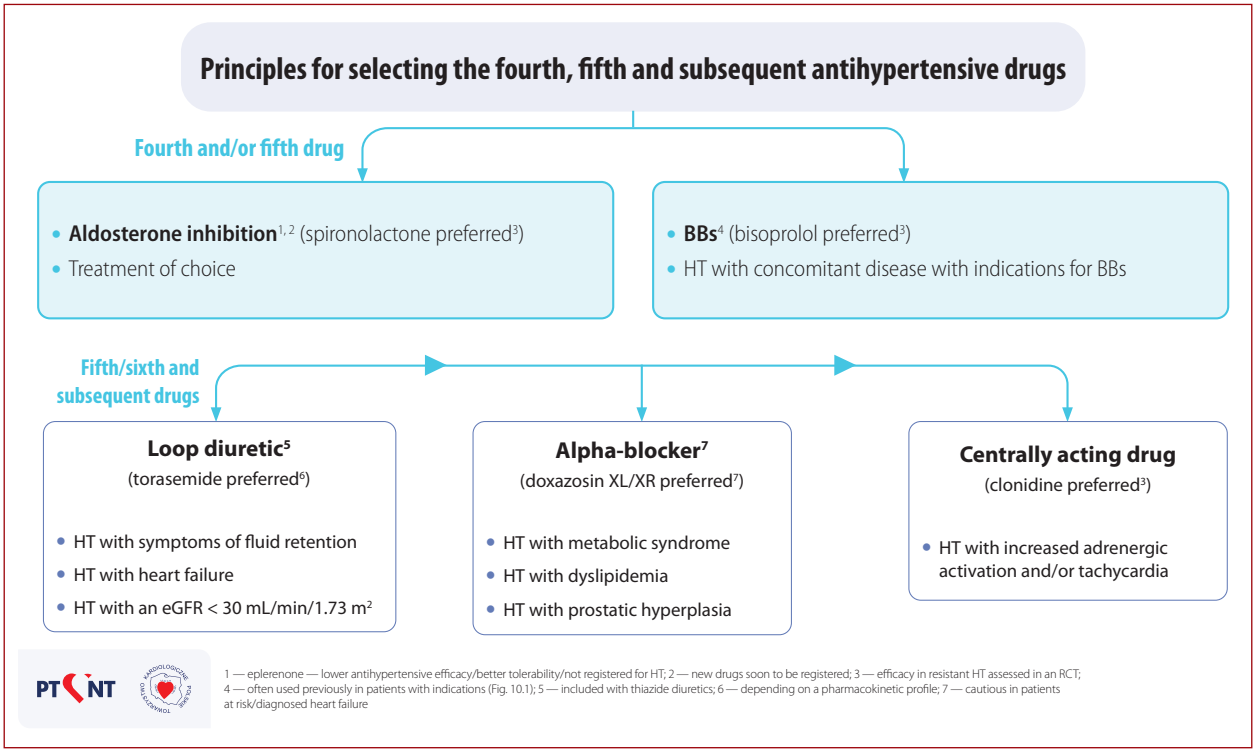


Figure 14.2. Algorithm for the treatment of resistant hypertension (HT)

section 4.7) [2, 4, 5, 268]. This diagnostic step is carried out in parallel with intensification of antihypertensive therapy for resistant HT.

14.3. Antihypertensive therapy of truly resistant HT

For truly resistant HT, a fourth antihypertensive drug should be added. According to current recommendations, aldosterone-inhibiting drugs and BBs are recommended (Figure 14.2). The treatment of choice is the use of MRAs, especially spironolactone, even at low doses (25–50 mg/day). In the PATHWAY-2 study, spironolactone was shown to have a stronger antihypertensive effect than bisoprolol or doxazosin [275]. Its effect can be attributed to the inhibition of aldosterone, the concentration of which is often elevated in resistant HT (increased secretion after an initial reduction due to renin-angiotensin system blockade or undiagnosed

primary hyperaldosteronism). In patients with an eGFR below 45 ml/min/1.73 m^2 or a potassium concentration of more than 4.5 mmol/l, spironolactone should be used with caution due to the risk of hyperkalemia. If spironolactone is not tolerated, eplerenone may be an alternative, although it is not currently registered for the treatment of HT and its efficacy is significantly lower [2, 4, 276]. Approval of the selective aldosterone synthesis inhibitor, baxdrostat, which has shown efficacy in the BrighHTN trial in patients with resistant HT can be expected soon [277]. Due to the high incidence of cardiac complications in resistant HT, BBs, especially bisoprolol, are also a recommended fourth drug [275, 278]. In clinical practice, patients with indications for BBs receive them earlier. It has been shown to be effective in intensifying ineffective therapy based on three essential drugs with an SPC containing four antihypertensive drugs using bisoprolol — ACEIs, TLDs/TDs, CCBs and BBs [279]. A vasodilating BB such as nebivolol (10 mg dose) may also be considered for selection.

In subsequent treatment steps, an increase in the number of drugs to five-seven may be considered, including:

- a loop diuretic (torasemide preferred) as an adjunct to TLDs/TDs (chlortalidone in patients with an eGFR <30 ml/min/1.73 m^2), especially in patients with CKD or with signs of sodium and water retention [4, 5, 48, 157];
- an alpha-blocker (doxazosin XL preferred) [270];
- a centrally acting drug (clonidine preferred) [280];
- a direct vasodilator (dihydralazine) [2, 4, 5, 268];
- a double endothelin inhibitor (aprocicentan), whose moderate efficacy was shown in the PRECISION trial [281].

In patients with resistant HT, drugs often need to be administered twice daily. In the case of refractory HT, which cannot be controlled despite treatment with five to seven drugs, and in the case of suspected secondary forms of HT, patients should be referred to a specialist HT centre [282]. In Poland, the diagnosis of resistant HT allows the patient to access priority hospital treatment within the National Cardiac Network.

15. INTERVENTIONAL TREATMENT OF HT

Renal artery denervation stands out among interventional treatments for HT in terms of the greatest evidence of antihypertensive efficacy from clinical trials, including those in which sham surgery was performed. However, there is a lack of data on its long-term efficacy, especially in terms of cardiovascular risk reduction [283–288]. Also worth noting are domestic studies on the efficacy of cardioneuromodulation in BP lowering. The cardioneuromodulation is the alghorithm available on a pacemaker that affects the autonomic system through changes in the PQ interval. This method requires further research [289].

Currently, only in centres with suitably experienced staff renal artery denervation can be considered as a therapeutic option, in patients with HT uncontrolled with at least three drugs in full doses, including TDLs/TDs. The decision to perform the procedure is made by a team of specialists, consisting of a hypertensiologist and an interventional cardiologist, after a detailed discussion with the patient about the potential benefits and risks. The procedure is not recommended in patients with an eGFR below 40 ml/min/1.73 m^2 [4, 5].

Although patients with an eGFR below 40 ml/min/1.73 m^2 were not eligible for randomized trials with the sham procedure, the results of observational studies demonstrate the safety and nephroprotecitive effect of the procedure in patients with CKD.

In patients who do not adhere to therapeutic recommendations or who cannot tolerate many antihypertensive drugs, especially the three essential ones, are at least at high cardiovascular risk and have not achieved target BP values, renal denervation may also be considered. The prerequisite is that patients are willing to undergo this procedure following a shared decision-making process. This process requires that patients are fully informed of the benefits, limitations and risks of renal denervation [5].

The issue of renal artery denervation will be discussed in detail in a forthcoming position paper of PTK and PTNT experts.

16. IMPORTANCE OF PATIENT CO-OPERATION IN LONG-TERM BP CONTROL

Non-adherence to therapeutic recommendations, including both lifestyle modifications and pharmacotherapy, is increasingly recognized as a major cause of failure to achieve therapeutic goals. This leads to increased morbidity and mortality from cardiovascular causes and increases healthcare costs, i.a. avoidable hospitalisations. This problem particularly concerns HT [290].

Two groups of patients are particularly vulnerable: the young and middle-aged, who, according to research, show the least persistence with therapy, and those who are just starting therapy with cardiovascular risk reducing drugs, including antihypertensive drugs. Early discontinuation of such treatment, for example with antihypertensive drugs and statins, is associated with a higher risk of morbidity and death from cardiovascular causes [291–293].

To increase adherence to treatment in cardiovascular diseases, there are several key areas to focus on. Improving communication skills and building a partnership between patient and clinician are a key. This allows for a fully informed decision by the patient and acceptance of the actions taken. Patient education, dispelling myths and misinformation from the internet, and the use of electronic reminder methods such as SMS can help. Eliminating economic barriers and monitoring treatment progress are also important. Simplifying treatment regimens through SPCs also promotes better adherence [294–296].

Multidirectional interventions to improve adherence, including building physician–patient partnerships so that all therapeutic decisions are autonomously made by the patient, can significantly increase treatment persistence

and reduce morbidity and mortality from cardiovascular causes in society.

17. EDITORIAL COMMITTEE, OPINION COMMITTEE AND REVIEWERS

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