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ARTYKUŁ SPECJALNY / *STATE-OF-THE-ART REVIEW*

Comparison of hypertension epidemiology and treatment in Poland and Australia

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INTRODUCTION

Hypertension remains the leading preventable worldwide cause of premature cardiovascular (CV) morbidity and mortality. The risk for stroke, heart disease, and kidney and peripheral damage increases in a linear fashion with blood pressure (BP) levels across all age groups in both men and women. Although the benefits of reducing major CV events through BP control are well-recognised, the management of hypertension continues to be a major global challenge. The unmet need for improvements in hypertension detection and treatment have been raised globally, resulting in the multinational Prospective Urban Rural Epidemiology (PURE) study [1]. Amongst 142,042 adults from 628 communities including high-income, upper-middle, low-middle and low-income countries, only 46.5% of participants were aware of their high BP levels, of whom less than half (40.6%) were receiving antihypertensive treatment, and only one in three (13.2%) individuals had achieved BP control < 140/90 mmHg [1]. The global disparities in hypertension prevalence, awareness, treatment, and control have been further detailed in a recent meta-analysis of 135 population-based studies including 968,419 adults from 90 countries [2]. In 2010, 31.1% of the worldwide adult population had elevated BP with a higher age-standardised prevalence of hypertension in low and middle-income countries (31.5%) compared to high-income countries (28.5%). Globally, the number of adults with hypertension reached an estimated total of 1.39 billion in 2010, including 349 million in high-income countries and 1.04 billion in low and middle-income countries. The highest prevalence and increase in prevalence of raised BP has been observed particularly in East Asia and the Pacific, Latin America and the Caribbean, South Asia, and sub-Saharan Africa. The 2017 report from the American Heart Association has indicated that the worldwide burden of hypertension is on the rise and is expected to increase even further due to substantial population growth and aging [3].

Numerous risk factors including age, race/ethnicity, family history, genetic factors, lower education and socioeconomic status, lower physical activity, tobacco use, physical stressors, and dietary habits (dietary fats, higher sodium intake, lower potassium intake, excessive alcohol intake) contribute to the development of elevated BP and poor BP control. A large proportion of the incidence of hypertension can be prevented by controlling dietary and lifestyle habits. Certainly, early detection of hypertension, associated CV risk factors, and subclinical organ damage with the use of antihypertensive medication to achieve strict BP control can reverse or help to effectively reduce hypertension-related cardiac, renal, vascular, and cerebrovascular complications. Conversely, unawareness of hypertension and insufficient treatment as a result of physician therapeutic inertia or patient non-compliance contribute to poor BP control and resultant adverse CV and renal outcomes. Therefore, identification of patients who are at high risk for further disease progression and associated complications from elevated BP is integral in daily clinical practice. Hypertension guidelines using rigorous evidence-based methods are designed to guide healthcare professionals with the latest results derived from hypertension trials and meta-analyses regarding BP control and treatment strategies. Most countries within their own hypertension societies follow the recent recommendations of the Eighth Joint National Committee (JNC 8) [4] and the 2013 European Society of Hypertension and the European Society of Cardiology (ESH/ESC) [5] and publish

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their own guidelines, which are adapted for the prevalence of the condition, drug availability, ethnicity-related factors, and government health policies locally. Amongst hypertension societies, the National Heart Foundation (NHF) of Australia is the first to release its updated 2016 guidelines for the diagnosis and management of hypertension in adults [6] based on recent evidence rated according to the National Health and Medical Research Council, recent hypertension clinical drug trials including the results of the Systolic Blood Pressure Intervention Trial (SPRINT) study, and the latest development of treatment strategies and treatment targets for selected hypertension-associated co-morbidities (i.e. stroke, chronic kidney disease, diabetes, myocardial infarction, heart failure [HF], and peripheral arterial disease).

EPIDEMIOLOGY OF ARTERIAL HYPERTENSION IN AUSTRALIA

Australia is ranked among the top four countries in relation to ageing and life expectancy. Nevertheless, cardiovascular disease (CVD) is a major cause of death in Australia, particularly in regional and rural areas [7], with more than double the age-standardised death rate from ischaemic heart disease in Aboriginal and Torres Strait Islander peoples when compared to non-Indigenous Australians [8]. Notably, in Australia in 2010, 7% of the total disease burden and 48% of CVD burden were attributable to hypertension. In the years 2014–2015, nearly 6 million Australians (34%) aged 18 years and over had elevated BP, defined as BP levels ≥ 140/90 mmHg or taking anti-hypertensive medication. More than 4.1 million people (68%) from this cohort had uncontrolled or untreated hypertension. The proportion of Australians with high BP was greater in men (24.4%) compared to women (21.7%) and showed an increase with ageing for both genders. Based on the Heart Foundation Heart Watch survey, in 2016, approximately 32.5% of people had been told by a doctor that they had raised BP, of whom more than half (59.9%) were taking BP-lowering medication. This survey also found that the lower the household income, the greater the likelihood of higher BP. The prevalence of hypertension was greater amongst Australians living in regional areas (33.9%) compared to their metropolitan counterparts (32%). Compared with non-Indigenous Australians, age-standardised prevalence of hypertension is 16% higher in Aboriginal and Torres Strait Islander peoples. The presence of other CV risk factors including smoking, obesity, and sedentary lifestyle is more prevalent amongst Indigenous Australians. In fact, Aboriginal and Torres Strait Islander adults were 70% more likely to die from CVD compared to non-Indigenous Australians.

EPIDEMIOLOGY OF ARTERIAL HYPERTENSION IN POLAND

The demographic distribution of hypertension is more unified in Poland, with far less geographical variation prevalence when compared to Australia. The incidence and control of elevated BP in Poland is largely based on the NATPOL 2011 survey, which included a representative sample of 2413 randomly selected Polish adults aged 18–79 years [9]. In this study, in line with diagnostic criteria as per Polish and European hypertension guidelines, arterial hypertension was determined on the basis of the average of three BP readings taken during each of two separate visits. Amongst 1168 men (mean age 44.9 ± 16.0 years) and 1245 women (mean age 46.7 ± 17.2 years) included in the NATPOL 2011 survey, 32.5% of Polish adults demonstrated hypertension. The percentage of subjects with optimal, normal, and high BP was 36.0%, 18.5%, and 12.5%, respectively. The prevalence of hypertension was significantly higher in men (36.8%) than in women (29.4%) and was shown to increase with age. In fact, 11.2% of adults aged 18–39 years were diagnosed with hypertension, 39.3% of those aged 40–59 years, and the highest peak at 67.8% was seen in individuals aged 60–79 years. The vast majority of patients demonstrated stage 1 hypertension (79.5%) as opposed to stage 2 (16.0%) and stage 3 hypertension (4.5%). However, the overall prevalence of hypertension has increased when compared to the NATPOL 2002 survey (30%), and BP control has improved from 12% in 2002 to 26% in 2011. Data on hypertension prevalence, awareness, and control in the elderly and very elderly comes from the PolSenior study [10]. This cross-sectional representative survey included a total of 4950 participants aged 65–104 years, equally distributed in six age subgroups. BP levels ≥ 140/90 mmHg were found in 78.2% of women and 70.1% of men. The highest prevalence of hypertension was noted in men aged 70–74 years (77.8%) and women aged 74–79 years (83.2%). Awareness of hypertension decreased from 80 years of age; however, elderly women were more aware of hypertension than men. The PolSenior study found a decreased rate in hypertension awareness and treatment with advanced age indicating a reverse trend in the prevalence and control of hypertension in individuals aged 80 years and older when compared to the younger elderly. In Poland, the burden of CVD and associated mortality attributable to hypertension is still high and remains a major public health challenge (Fig. 1).

GUIDELINES FOR ARTERIAL HYPERTENSION MANAGEMENT

The current guidelines for the diagnosis and management of hypertension in adults emphasise the role of absolute CVD risk assessment for asymptomatic Aboriginal and Torres Strait Islander peoples aged > 35 years and non-Indigenous Australians > 45 years of age with unknown CVD. Among several tools to help clinicians with the estimation of absolute risk for primary prevention is a calculator developed by the National Vascular Disease Prevention Alliance, which assesses an individual's risk of developing a CV event over a five-year period. The risk for the individual is based on sex, age, systolic BP (SBP), smoking status, total cholesterol and high-density lipoprotein (HDL) levels, the presence of diabetes, and elec-

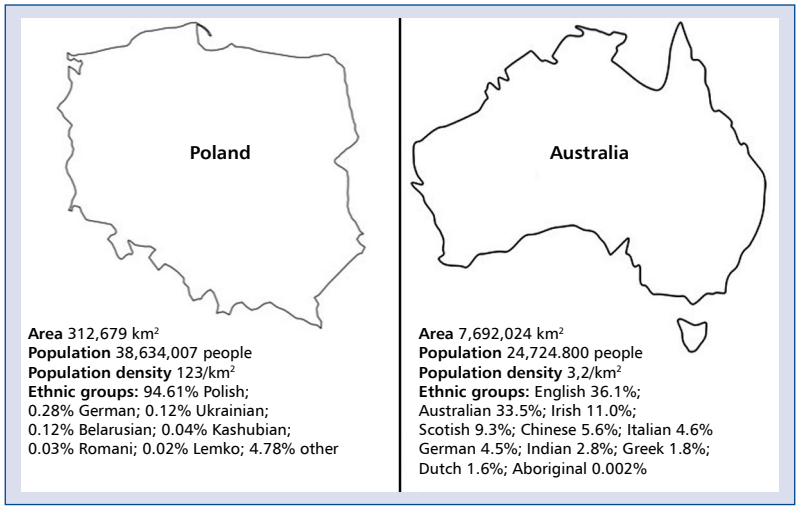

Figure 1. Comparison between Australia and Poland in terms of ethnic structure. Based on: *Powierzchnia i ludność w przekroju terytorialnym w 2011 r. 1. Departament Metodologii, Standardów i Rejestrów*. [Area and population in territorial cross-section in 2011 1. Department of Methodology, Standards and Registers]. GUS. On-line 2017-11-19; and Australian Bureau of Statistics, Australian Demographic Statistics, Mar 2017, www.abs.gov.au. On-line 2017-11-19

trocardiogram (ECG) left ventricular hypertrophy and provides an estimated percentage risk score (low < 10%, moderate 10–15%, high > 15%). Patient management delivered by the healthcare professional is based on the risk score outcome and includes lifestyle advice, diagnostic investigations or the initiation of treatment. Characteristics considered to be high risk in Australia include age (adults > 60 years old or Indigenous Australians > 74 years old), diabetes, microalbuminuria, estimated glomerular filtration rate < 45 mL/min/1.73 m^2, grade 3 hypertension, familial hypercholesterolaemia, or serum total cholesterol > 7.5 mmol/L.

Guidelines of the Polish Society of Hypertension (*Polskie Towarzystwo Nadciśnienia Tętniczego* [PTNT]) and the ESH/ESC [5] also highlight the role of the total CV risk assessment [11]. Decision on initiation therapy and the choice of treatment is always based on the risk stratification. In numerous European countries including Poland, the Systematic Coronary Risk Evaluation (SCORE) model estimates the risk of death from CVD (not just coronary heart disease or event) over a 10-year period based on age, gender, smoking habits, total cholesterol, and SBP. The SCORE risk chart is highly dependent on age, so in younger adults with elevated BP total absolute CV risk can be underestimated in the presence of additional risk factors or asymptomatic organ damage. Therefore, the hypertension guidelines for the management of hypertension recommend the assessment of CV risk based on BP category, CV risk factors influencing prognosis, asymptomatic organ damage, and presence of diabetes, symptomatic CVD, or chronic kidney disease [5].

BLOOD PRESSURE MEASUREMENTS

The current Australian guidelines emphasise the importance of out-of-clinic BP measurements with the use of ambulatory BP monitoring and home self-reported BP assessment. Evidence from numerous results from systematic reviews and meta-analyses has demonstrated the prognostic values of ambulatory and home BP on CV outcomes above and beyond clinic BP.

In office clinic BP measurements, the Australian guidelines highlight the importance of unobserved (unattended) automated office BP (AOBP), a key change from the previous guideline. AOBP is performed without the presence of a healthcare professional, thereby eliminating many of the causes of inaccurate office BP readings, minimising white coat hypertension effects, thereby resulting in markedly lower BP readings when compared to conventional clinic BP [12, 13]. AOBP can be measured with the BpTRU or the HEM-907 BP monitor available in Australia. AOBP has been found to be superior to semi-automated BP recorders and provides comparable recordings to the awake ambulatory and home BP [14]. The principles of the AOBP method have been applied in the recent randomised controlled open-label SPRINT study [15]. In this study, a total of 9361 patients aged 50 years or older with SBP > 130 mmHg or higher and an increased CV risk (without diabetes, previous stroke or HF) were randomised to an intensive treatment to achieve SBP target < 120 mmHg or a standard treatment to attain SBP target < 140 mmHg. The primary composite outcome was myocardial infarction, acute coronary syndromes, stroke, HF, or death from CV causes [15]. Following one year of therapy, the mean SBP was 121.4 mmHg in the intensive-treatment group and 136.2 mmHg in the standard-treatment group. This study was terminated early (median follow-up of 3.26 years) due to a significant reduction of primary efficacy endpoints by 25% and the risk of death from all causes by 27% in the

intensive-treatment group compared to the standard-treatment group. However, a more aggressive treatment led to higher rates of serious adverse events of hypotension, syncope, electrolyte abnormalities, and acute kidney injury or failure, but not of injurious falls when compared to the standard-treatment group [15]. A subgroup analysis of the SPRINT patients (n = 2636) > 75 years of age revealed a significant reduction of primary composite outcomes by 33% and all-cause mortality by 32% in the group with lowered SBP < 120 mmHg when compared to the group with SBP < 140 mmHg [16]. The overall serious adverse events (i.e. hypotension, electrolyte abnormalities, acute kidney injury and injurious falls) were comparable between both treatment arms.

The assessment of AOBP using the HEM 907 device is crucial when interpreting the results of the SPRINT trial. A recent study of a total of 353 hypertensive patients documented that AOBP with BpTRU was –15/–8 mmHg lower than office conventional auscultatory method and –10/–4 mmHg when compared to home BP [17]. These findings suggest that the treatment arm (< 120 mmHg) in the SPRINT is likely to translate into the SBP of ~135 mmHg, which remains within the current recommended SBP threshold of less than 140 mmHg [18].

The Polish hypertension guidelines recommend the measurement of BP with the use of three methods: (1) office BP monitoring (OBPM) — performed by a healthcare professional in the clinical settings; (2) home BP monitoring (HBPM), which is a self-performed method used outside of the clinic; and (3) ambulatory BP monitoring (ABPM), which is an automated long-term BP assessment [11]. The AOBP approach for BP measurements has not yet been included in the Polish guidelines. The PTNT guidelines are primarily based on standardised OBPM for the diagnosis of hypertension, its stage, and BP treatment threshold. Notably, the Polish guidelines were among the first to include ABPM into the diagnostic scheme. In patients suspected of having hypertension with BP values < 160/100 mmHg, the diagnosis of hypertension should be confirmed by ABPM or, if this is not available, by HBPM. ABPM is superior method of assessment when compared to clinic or home BP readings, as it provides data on diurnal BP profile including its variability, morning surge, and dipping pattern.

BLOOD PRESSURE TREATMENT TARGETS

Following the positive outcomes of SPRINT, the NHF Australian guidelines consider a more aggressive treatment regime aiming for a target of SBP < 120 mmHg in selected high CV risk patients in whom therapy is well tolerated and seems to be safe. However, this approach requires close monitoring in regard to potential treatment-related effects (i.e. hypotension, syncope, electrolytes, renal injury, etc.). In uncomplicated hypertension, according to the NHF guidelines, the treatment target is to achieve BP control < 140/90 mmHg or lower if tolerated. A BP target < 140/90 mmHg is also recommended for hypertensive patients with diabetes, chronic kidney disease, and history of transient ischaemic attacks or stroke.

Despite improvements in CV outcomes as a result of a more aggressive treatment with a target SBP < 120 mmHg (20 mmHg lower than SBP threshold as recommended by all international and national hypertension guidelines), the PTNT found that there was not enough evidence to verify the existing guidelines, which have been comprehensively justified in the Commentary to the SPRINT in the 'Arterial Hypertension' [19]. The target BP levels according to Polish guidelines remains < 140/90 mmHg for the vast majority of hypertensive patients, including those with CV complications, and < 140/85 mmHg for diabetes and < 150 mmHg for adults > 80 years of age [11].

ANTIHYPERTENSIVE DRUGS CHOICE

In grade 1 essential hypertension, a single antihypertensive drug results in a BP lowering effect of not more than 20/10 mmHg in an estimated two-thirds of hypertensive patients [11]. A large number of randomised controlled trials and meta-analyses to date have demonstrated that all antihypertensive drug classes produce a significant reduction in stroke and major CV events, indicating that improvements in outcomes are more due to BP lowering *per se* rather than specific drug properties [20]. However, evidence for risk reduction of other events and mortality has been obtained with some drug classes only. Furthermore, a meta-analysis of the head-to-head comparisons of different classes of agents revealed significant differences among drug classes. When all antihypertensive classes are compared, diuretics are superior in preventing HF, beta-blockers are less effective in preventing stroke, and calcium antagonists superior in preventing stroke and all-cause death but inferior in preventing HF, angiotensin-converting enzyme inhibitors (ACEI) are more effective in preventing coronary heart disease and less effective in preventing stroke; angiotensin receptor blockers (ARB) are inferior in preventing coronary heart disease, and renin–angiotensin system (RAS) blockers are more effective in preventing HF. While these findings are unable to provide a fixed paradigm of favourable drug choice for all hypertensive patients, it may suggest specific choices or preferable combinations of drugs in particular conditions [21].

In this context, the Australian NHF guidelines are based on evidence associated with drug classes rather than an individual agent, and the initial drug choice takes into consideration age, the presence of end-organ damage and associated clinical conditions, potential interaction with other drugs, patient adherence, and drug cost. In view of comparable effectiveness on BP reduction, first-line therapy using single-drug treatment in uncomplicated hypertension can be initiated either with thiazide diuretics, calcium channel blockers, ACEI, or ARB but not beta-blockers as per the NHF guideline.

The 2015 PTNT guidelines are more detailed in this context and highlight that the benefits with first-line therapy in uncomplicated hypertension are not only related to BP lowering effect *per se* but specific drug choice [11]. Particular consideration should be given to a long-acting drug (once daily therapy) with a high trough-to-peak ratio, which provides steady and diurnal BP control and better long-term CV protection, minimises daytime BP variability and drug intolerance (commonly associated with short-acting drugs), and improves patient adherence.

Further to this, if possible, first-line therapy should consider mechanisms underlying uncomplicated essential hypertension with a preference of first drug choice for the RAS blockade or beta-blockers in younger adults in whom higher levels of plasma renin, renal sympathetic tone, and cardiac output (hyperkinetic hypertension) are commonly present [11]. Thiazide or thiazide-like diuretics and calcium channel blockers are preferable in older adults who often demonstrate low renin hypertension, hypervolaemia, and structural vascular changes including arterial stiffness.

Most importantly, if a target BP is not achieved with monotherapy, further titration of a single drug may not produce sustained BP reduction, but it substantially increases the risk of drug-induced side effects. Therefore, a second preferred drug class with different mechanisms of action should be commenced. This is in line with the Australian guidelines, which recommend that if the target BP is not achieved within three months, a second drug from a different pharmacological class at low-moderate dose, rather than increasing the dose of the first drug, should be initiated to maximise antihypertensive efficacy. For initial dual therapy in uncomplicated hypertension, the NHF guidelines advise combination drug therapy of ACEI and calcium channel blockers over a diuretic combined with either ACEI or beta-blocker.

Previous clinical trials found that aggressive early treatment of hypertension may preclude further development of treatment resistance in high-risk hypertensive patients [22, 23]. Initiating therapy with two drugs in combination produces more prompt achievement of BP control and translates into better CV outcomes compared to initial single-drug therapy. A retrospective analysis of 1762 patients with stage 1 hypertension has documented that initial combination therapy was associated with a significant reduction of CV events as a result of faster achievement of target BP than initiating monotherapy and later switching to combination therapy [24]. Further support for the improvement of early effectiveness in achieving BP control with the use of initial combination therapy comes from the randomised parallel-group ACCELERATE study of patients with stage 1 and 2 hypertension [25]. Patients treated with an initial combination of both aliskiren and amlodipine had substantially better mean BP reduction over the first 24 weeks when compared to patients starting on either drug as monotherapy. Moreover, when the monotherapy patients were switched to combination therapy, a further decrease in BP was noted. However, sequential add-on treatment with the same type of drug has never numerically matched the levels of the initial combination group. Whether early versus delayed combination therapy should be considered in mild stage 1 uncomplicated hypertension remains to be determined. Currently, the ESH/ESC hypertension guidelines recommend starting the combination therapy with SBP ≥ 160 mmHg or diastolic BP ≥ 100 mmHg in uncomplicated hypertension.

CHOICE OF ANTIHYPERTENSIVE DRUGS

Beta-blockers

The Polish and Australian guidelines for the treatment of elevated BP differ primarily around the use of beta-blockers. The NHF guidelines do not recommend the use of atenolol monotherapy due to poor outcomes as determined in previous meta-analyses; however, in drug combination treatment, atenolol and metoprolol are the most commonly prescribed beta-blockers for the management of uncontrolled hypertension in Australia. Highly selective, long-acting beta-blockers such as betaxolol or bisoprolol are not used for hypertension management in Australia, with use of carvedilol, bisoprolol, nebivolol, or metoprolol recommended only post-myocardial infarction or in HF patients. Conversely, the 2011 PTNT guidelines emphasise a preference for the use of beta-blockers with vasodilator activity (i.e. celiprolol, carvedilol, nebivolol) in uncomplicated hypertension, particularly in the presence of metabolic abnormalities and diabetes. The vasodilation properties of beta-blockers result in beneficial effects on metabolic profile, endothelial function, haemodynamics (central BP), and regression of end-organ damage (i.e. left ventricular hypertrophy, microalbuminuria). Long-acting beta-1 cardioselective beta-blockers (i.e. betaxolol, bisoprolol) are a preferable treatment option for younger adults with hyperkinetic hypertension and young females of reproductive age.

Clearly, uncomplicated hypertension and the vast majority of hypertension complicated by associated co-morbidities (with the exception of pregnancy hypertension) should be treated in monotherapy or combination with the use of five antihypertensive drug classes that have documented evidence of producing a reduction in CV morbidity and CV death.

Other hypertensive drug classes in uncontrolled hypertension

Robust evidence from prospective clinical trials on the impact of alpha-blockers, aldosterone antagonists, loop diuretics, centrally acting drugs, or vasodilators on CV morbidity and mortality is lacking and precludes their use as the first- or second-line therapy for hypertension management. Nevertheless, their therapeutic effectiveness in lowering BP is well-recognised in the treatment of resistant hypertension (RH). It has been reported that 10.1% of patients treated for elevated BP failed to attain target BP levels despite widespread

use of conventional antihypertensive therapy [26]. According to cross-sectional analysis of the United States National Health and Nutrition Examination Survey (NHANES), the prevalence of patients who met the criteria for RH (defined by systolic and diastolic BP ≥ 140/90 mmHg and reported use of three different drug classes or drugs from ≥ four antihypertensive drug classes irrespective of BP levels) has doubled, reaching 11.8% in 2006 compared to 5.5% in the years 1998–2004 [3]. A recent systematic review and meta-analysis of 20 observational studies and four randomised controlled trials with a total of 961,035 treated hypertensive patients documented that the pooled estimated prevalence of RH is 13.7% [27]. However, most of these studies measured apparent resistance, so the exact prevalence of RH still needs to be determined by the uniform definition of RH, standardisation of BP measurements (confirmed by ambulatory recordings), exclusion of pseudo-resistance and secondary hypertension, confirmation of medication compliance, and drug dosage [27].

More recent evidence including the hypertension guidelines suggests the use of spironolactone as a fourth-line therapy for the treatment of true RH followed by the triple combination of an renin–angiotensin–aldosterone blocker, a calcium channel blocker, and a diuretic at maximum tolerated doses. The use of an aldosterone receptor antagonist is supported by the concept that sodium retention is a contributing factor to the pathophysiology of RH. This hypothesis was tested in the PATHWAY-2 trial, the first double-blind, placebo-controlled randomised crossover trial in patients with confirmed RH, despite at least three months of triple antihypertensive therapy with maximally tolerated doses (an ACEI or an ARB, a calcium channel blocker, and a diuretic) [28]. At three-month follow-up all patients were rotated through four cycles of once-daily oral treatment (with a randomly ordered sequence of drugs) with spironolactone (25–50 mg), doxazosin modified release (4–8 mg), bisoprolol (5–10 mg), and placebo. This study demonstrated that spironolactone was the most effective BP lowering treatment between baseline and a 12-week period (–14.4 mmHg) when compared to placebo (–4.2 mmHg), doxazosin modified release (–9.1 mmHg), and bisoprolol (–8.4 mmHg) in the treatment of RH as documented by home BP [28]. All drugs were well tolerated; however, in six out of 285 patients serum potassium exceeded 6.0 mmol/L on one occasion following spironolactone. While gynaecomastia was not observed in this cohort due to the short study duration, it is possible that long-term therapy induces the associated side effects. The extension of the PATHWAY-2 study currently underway will determine whether amiloride is an effective alternative to spironolactone in patients with RH. Findings from the PATHWAY-2 trial have established a clear drug-hierarchy therapy, which is likely to influence future treatment guidelines, clinical practice globally, and redefinition of RH.

Further promising approaches for the treatment of RH include the use of sequential nephron blockade as an add-on therapy. The use of three dissimilar diuretics (e.g. spironolactone, furosemide, amiloride) acting at different nephron segments added to the standardised triple-drug combination (irbesartan, hydrochlorothiazide, and amlodipine) resulted in a greater reduction in ambulatory BP when compared to add-on sequential RAS blockade (e.g. ramipril, bisoprolol) [29]. While the use of sequential nephron blockade seems to target pathophysiology of RH via blocking sodium retention, it is possible that this approach may trigger counter-regulatory mechanisms over the longer-term further potentiation of sympathetic activation and drug resistance. Therefore, longer-term studies are required prior to commencing this approach to clinical practice for the management of uncontrolled BP.

Centrally acting agents, including clonidine, moxonidine, rilmenidine, and methyldopa, via stimulation of alpha-2 receptors and/or imidazoline receptors on adrenergic neurons located in the rostral ventrolateral medulla produce sympathetic outflow inhibition. These drugs favourably modulate centrally-mediated efferent sympathetic outflow, thereby more directly targeting potentiated sympathetic activation in RH [30] likely to overcome central resistance to conventional antihypertensive medication. While centrally acting drugs are less tolerated due to associated side effects including symptoms of dry mouth, somnolence, dizziness, and others, this is less common with the use of rilmenidine or moxonidine therapy. Nevertheless, effects on CV outcome and mortality have not yet been established in hypertension. Moxonidine is a commonly used drug as an add-on therapy for the treatment of RH in Australia. Rilmenidine is available in Poland but is not commonly used when compared to methyldopa, a short-acting drug with a dose-dependent BP lowering effect, and not often tolerated at maximum antihypertensive doses due to its side-effects.

The alpha-1-blocker doxazosin has been found to be a safe and effective BP lowering therapy [31] and is currently used in multi-drug regimens for the treatment of RH [5]. The side effects associated with doxazosin including dizziness, fatigue, and headache can be minimised by the use of a modified-release dosage (4 or 8 mg) at evening time to prevent orthostatic hypotension. The PTNT guideline recommends the use of doxazosin in patients with RH and tamsulosin with preferential selectivity for the alpha-1A-adrenergic receptor in the prostate of patients with benign prostatic hyperplasia and hypertension that requires therapy with no more than two antihypertensive agents.

In Australia, doxazosin is not available, and a short-acting prazosin is used instead with initial dose 0.5 mg twice daily and titrated to 3–20 mg daily (in two or three doses), which is often less tolerated due to side effects and BP variation.

Future directions

Despite the availability of potent antihypertensive drugs, hypertension-related morbidity and mortality continue to

Table 1. Blood pressure value definitions according to the American Heart Association guidelines; DBP — systolic blood pressure; SBP — systolic blood pressure

		SBP [mmHg] →				
		< 120	120–129	130–139	140–159	160+
↓ DBP [mmHg]	< 80	Normal	Elevated	Stage 1	Stage 2	Stage 2
	80–89	Stage 1	Stage 1	Stage 1	Stage 2	Stage 2
	90–99	Stage 2	Stage 2	Stage 2	Stage 2	Stage 2
	100+	Stage 2	Stage 2	Stage 2	Stage 2	Stage 2

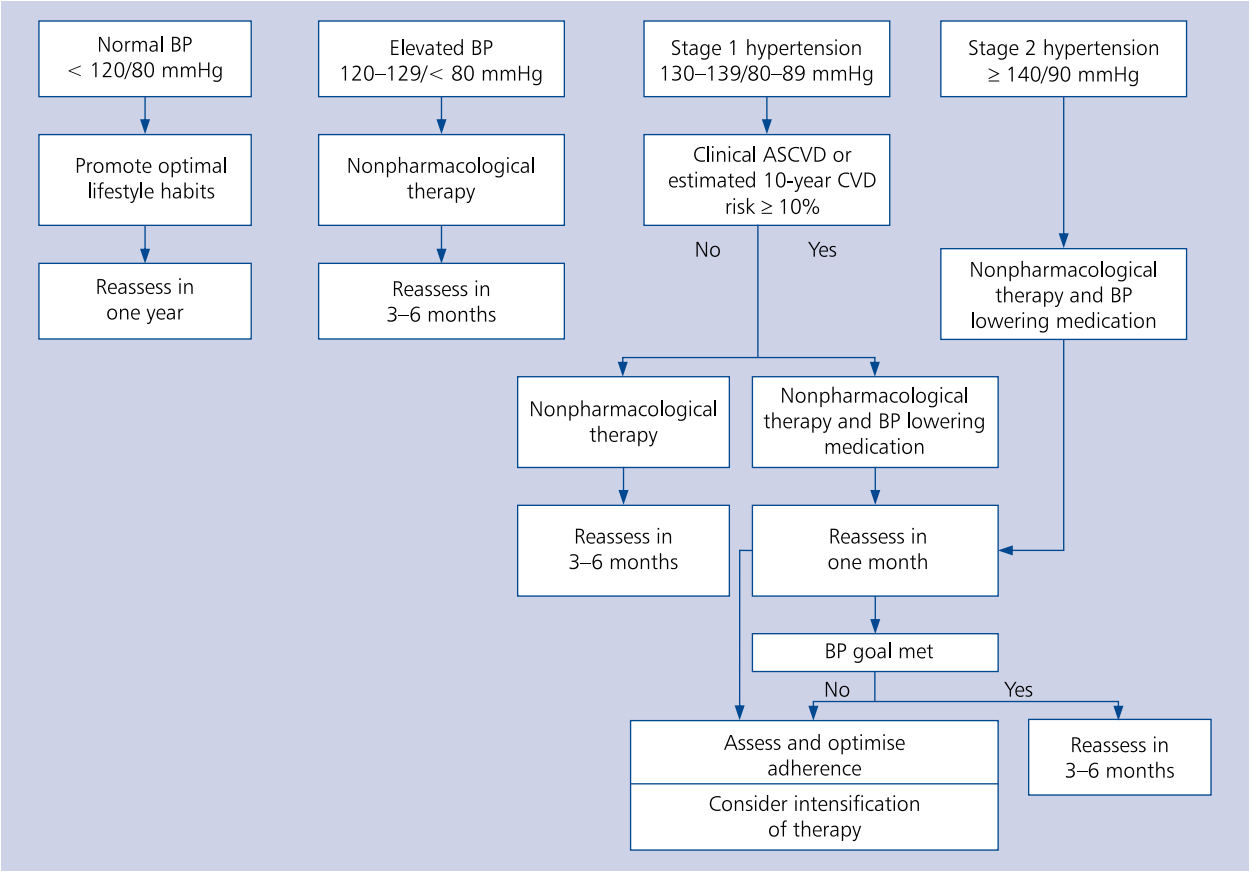

Figure 2. Arterial hypertension treatment according to the American Heart Association guidelines; ASCVD — atherosclerotic cardiovascular disease; BP — blood pressure; CVD — cardiovascular disease

rise globally. Improving early detection of hypertension, associated CV risk factors and disease management can considerably reduce the disease burden attributable to raised BP globally. Therapeutic physician inertia (i.e. insufficient or delayed antihypertensive treatment) and poor medication adherence as a result of insufficient patient knowledge and education regarding disease processes are major contributing factors to the inadequate management and control of BP. Attention should, therefore, be focused on optimising the initial antihypertensive drug strategy, standardising home BP measurements, and initiation of early patient involvement in disease management, including lifestyle changes. This will substantially improve adherence to treatment and allow BP control to be achieved in the vast majority of patients, thereby reducing the risk of further disease progression, associated adverse complications, and treatment resistance.

Identification and treatment of secondary hypertension are of utmost importance because in most cases removal of the underlying cause will result in BP control or normalisation, thereby reducing the CV risk and disease burden. Pseu-

do-resistance is clinically challenging; however, its diagnosis is a fundamental step in identifying RH. ABPM following the witnessed drug intake is crucial to truly confirm RH. Given that patients with RH at high CV and renal risk commonly display a high prevalence of organ damage when compared to age-matched patients with controlled hypertension, a multi-drug regimen including fourth-line therapy with an aldosterone antagonist and add-on therapy with a centrally acting agent can possibly overcome drug resistance. Those patients who remain truly RH may benefit from new alternative device-based therapies aimed at specifically modulating neural mechanisms involved in BP control. This, however, if relevant, should only be performed by a highly experienced staff in accredited hypertension treatment centres.

CONCLUSIONS

Although the Polish and Australian societies differ in terms of sociodemographic structure, the prevalence of elevated BP remains high in both countries, with the disease burden contributing to increased CV mortality and morbidity. Hypertension guidelines from both national societies share numerous common aspects derived from the same evidence-based studies. Differences exist regarding the choice and preference of specific hypotensive agents. Nevertheless, neither of the two guidelines are as up-to-date as the recently published guidelines of the American College of Cardiology (ACC) and the American Heart Association (AHA) [32]. The ACC/AHA have proposed a new definition for stage 1 hypertension, with a BP threshold of 130–139 mmHg for systolic or 80–89 mmHg for diastolic, which will further extend the disease burden (Table 1, Fig. 2). Moreover, the ACC/AHA guidelines also recommend a BP target of less than 130/80 mmHg for the management of hypertension. It is possible therefore that future Polish and Australian hypertension guidelines may follow suit, trending towards the earlier detection and more aggressive management of hypertension.

Conflict of interest: *none declared*

References

1. Chow CK, Teo KK, Rangarajan S, et al. Prevalence, awareness, treatment, and control of hypertension in rural and urban communities in high-, middle-, and low-income countries. JAMA. 2013; 310(9): 959–968, doi: 10.1001/jama.2013.184182, indexed in Pubmed: 24002282.
2. Mills KT, Bundy JD, Kelly TN, et al. Global Disparities of Hypertension Prevalence and Control: A Systematic Analysis of Population-Based Studies From 90 Countries. Circulation. 2016; 134(6): 441–450, doi: 10.1161/CIRCULATIONAHA.115.018912, indexed in Pubmed: 27502908.
3. Benjamin EJ, Blaha MJ, Chiuve SE, et al. American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart Disease and Stroke Statistics-2017 Update: A Report From the American Heart Association. Circulation. 2017; 135(10): e146–e603, doi:10.1161/CIR.0000000000000485, indexed in Pubmed: 28122885.
4. James PA, Oparil S, Carter BL, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). JAMA. 2014; 311(5): 507–520, doi: 10.1001/jama.2013.284427, indexed in Pubmed: 24352797.
5. Mancia G, Fagard R, Narkiewicz K, et al. Task Force Members. 2013 ESH/ESC Guidelines for the management of arterial hypertension: the Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). J Hypertens. 2013; 31(7): 1281–1357, doi: 10.1097/01.hjh.0000431740.32696.cc, indexed in Pubmed: 23817082.
6. Gabb GM, Mangoni AA, Arnolda L, et al. Guideline for the diagnosis and management of hypertension in adults - 2016. Med J Aust. 2016; 205(2): 85–89, doi: 10.5694/mja16.01132, indexed in Pubmed: 27456450.
7. Alston LV, Peterson KL, Jacobs JP, et al. A systematic review of published interventions for primary and secondary prevention of ischaemic heart disease (IHD) in rural populations of Australia. BMC Public Health. 2016; 16: 895, doi: 10.1186/s12889-016-3548-1, indexed in Pubmed: 27567666.
8. Nichols M, Peterson K, Herbert J, et al. Australian heart disease statistics 2015. National Heart Foundation of Australia. 2015.
9. Zdrojewski T, Rutkowski M, Gaciong Z, et al. Rozpowszechnienie, wykrywanie i skuteczność leczenia nadciśnienia tętniczego w Polsce — wyniki badania NATPOL 2011. Nadciśn Tętn. 2014; 18: 116–117.
10. Zdrojewski T, Wizner B, Więcek A, et al. Prevalence, awareness, and control of hypertension in elderly and very elderly in Poland: results of a cross-sectional representative survey. J Hypertens. 2016; 34(3): 532–8; discussion 538, doi: 10.1097/HJH.0000000000000823, indexed in Pubmed: 26771343.
11. Tykarski A, Narkiewicz K, Gaciong Z, et al. Zasady postępowania w nadciśnieniu tętniczym — 2015 rok. Wytyczne Polskiego Towarzystwa Nadciśnienia Tętniczego. [2015 guidelines for the management of hypertension. Recommendations of the Polish Society of Hypertension]. Nadciśn Tętn. 2015; 1(1): 1–70.
12. Myers MG, Campbell NRC. Unfounded concerns about the use of automated office blood pressure measurement in SPRINT. J Am Soc Hypertens. 2016; 10(12): 903–905, doi: 10.1016/j.jash.2016.10.003, indexed in Pubmed: 27863819.
13. Myers MG. Automated Office Blood Pressure-Incorporating SPRINT Into Clinical Practice. Am J Hypertens. 2017; 30(1): 8–11, doi: 10.1093/ajh/hpw086, indexed in Pubmed: 27551025.
14. Leenen F, Myers MG. Automated office blood pressure measurement in the management of hypertension - fourth in series. An article from the e-journal of the ESC Council for Cardiology Practice 10 Mar 2015.
15. Wright JT, Williamson JD, Whelton PK, et al. SPRINT Research Group. A Randomized Trial of Intensive versus Standard Blood-Pressure Control. N Engl J Med. 2015; 373(22): 2103–2116, doi: 10.1056/NEJMoa1511939, indexed in Pubmed: 26551272.
16. Williamson JD, Supiano MA, Applegate WB, et al. SPRINT Research Group. Intensive vs Standard Blood Pressure Control and Cardiovascular Disease Outcomes in Adults Aged ≥75 Years: A Randomized Clinical Trial. JAMA. 2016; 315(24): 2673–2682, doi: 10.1001/jama.2016.7050, indexed in Pubmed:27195814.
17. Filipovský J, Seidlerová J, Kratochvíl Z, et al. Automated compared to manual office blood pressure and to home blood pressure in hypertensive patients. Blood Press. 2016; 25(4): 228–234, doi: 10.3109/08037051.2015.1134086, indexed in Pubmed: 26852625.
18. Kjeldsen SE, Mancia G. Unobserved automated office blood pressure measurement in the Systolic Blood Pressure Intervention Trial (SPRINT): systolic blood pressure treatment target remains below 140 mmHg. Eur Heart J Cardiovasc Pharmacother. 2016; 2(2): 79–80, doi: 10.1093/ehjcvp/pvw002, indexed in Pubmed: 27533517.

19. Tykarski A. Badanie SPRINT — czy wytyczne leczenia nadciśnienia tętniczego PTNT 2015 wymagają weryfikacji w zakresie docelowych wartości ciśnienia tętniczego? Arterial Hypertension. 2016; 20(2): 1.
20. Thomopoulos C, Parati G, Zanchetti A. Effects of blood pressure lowering on outcome incidence in hypertension: 4. Effects of various classes of antihypertensive drugs--overview and meta-analyses. J Hypertens. 2015; 33(2): 195–211, doi: 10.1097/HJH.0000000000000447, indexed in Pubmed: 25485720.
21. Thomopoulos C, Parati G, Zanchetti A. Effects of blood pressure-lowering on outcome incidence in hypertension: 5. Head-to-head comparisons of various classes of antihypertensive drugs - overview and meta-analyses. J Hypertens. 2015; 33(7): 1321–1341, doi: 10.1097/HJH.0000000000000614, indexed in Pubmed: 26039526.
22. Julius S, Kjeldsen SE, Weber M, et al. VALUE trial group. Outcomes in hypertensive patients at high cardiovascular risk treated with regimens based on valsartan or amlodipine: the VALUE randomised trial. Lancet. 2004; 363(9426): 2022–2031, doi: 10.1016/S0140-6736(04)16451-9, indexed in Pubmed: 15207952.
23. Dahlöf B, Sever PS, Poulter NR, et al. ASCOT Investigators. Prevention of cardiovascular events with an antihypertensive regimen of amlodipine adding perindopril as required versus atenolol adding bendroflumethiazide as required, in the Anglo-Scandinavian Cardiac Outcomes Trial-Blood Pressure Lowering Arm (ASCOT-BPLA): a multicentre randomised controlled trial. Lancet. 2005; 366(9489): 895–906, doi: 10.1016/S0140-6736(05)67185-1, indexed in Pubmed: 16154016.
24. Gradman AH, Parisé H, Lefebvre P, et al. Initial combination therapy reduces the risk of cardiovascular events in hypertensive patients: a matched cohort study. Hypertension. 2013; 61(2): 309–318, doi: 10.1161/HYPERTENSIONAHA.112.201566, indexed in Pubmed: 23184383.
25. Brown MJ, McInnes GT, Papst CC, et al. Aliskiren and the calcium channel blocker amlodipine combination as an initial treatment strategy for hypertension control (ACCELERATE): a randomised, parallel-group trial. Lancet. 2011; 377(9762): 312–320, doi: 10.1016/S0140-6736(10)62003-X, indexed in Pubmed: 21236483.
26. Judd E, Calhoun DA. Apparent and true resistant hypertension: definition, prevalence and outcomes. J Hum Hypertens. 2014; 28(8): 463–468, doi:10.1038/jhh.2013.140, indexed in Pubmed: 24430707.
27. Achelrod D, Wenzel U, Frey S. Systematic review and meta-analysis of the prevalence of resistant hypertension in treated hypertensive populations. Am J Hypertens. 2015; 28(3): 355–361, doi: 10.1093/ajh/hpu151, indexed in Pubmed: 25156625.
28. Williams B, MacDonald TM, Morant S, et al. British Hypertension Society's PATHWAY Studies Group. Spironolactone versus placebo, bisoprolol, and doxazosin to determine the optimal treatment for drug-resistant hypertension (PATHWAY-2): a randomised, double-blind, crossover trial. Lancet. 2015; 386(10008): 2059–2068, doi: 10.1016/S0140-6736(15)00257-3, indexed in Pubmed: 26414968.
29. Bobrie G, Frank M, Azizi M, et al. Sequential nephron blockade versus sequential renin-angiotensin system blockade in resistant hypertension: a prospective, randomized, open blinded endpoint study. J Hypertens. 2012; 30(8): 1656–1664, doi: 10.1097/HJH.0b013e3283551e98, indexed in Pubmed: 22728905.
30. Martin U, Hill C, O' Mahony D. Use of moxonidine in elderly patients with resistant hypertension. J Clin Pharm Ther. 2005; 30(5): 433–437, doi:10.1111/j.1365-2710.2005.00672.x, indexed in Pubmed: 16164488.
31. Chapman N, Chang CL, Dahlöf B, et al. ASCOT Investigators. Effect of doxazosin gastrointestinal therapeutic system as third-line antihypertensive therapy on blood pressure and lipids in the Anglo-Scandinavian Cardiac Outcomes Trial. Circulation. 2008; 118(1): 42–48, doi:10.1161/CIRCULATIONAHA.107.737957, indexed in Pubmed: 18559700.
32. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Hypertension. 2017 [Epub ahead of print], doi: 10.1161/HYP.0000000000000066, indexed in Pubmed: 29133354.

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