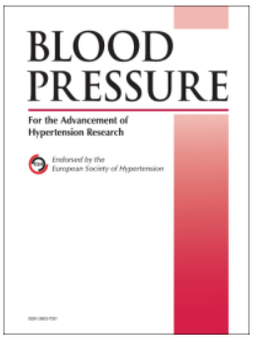

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Highlights of the 2023 European Society of Hypertension Guidelines: what has changed in the management of hypertension in patients with cardiac diseases?

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EDITORIAL

Highlights of the 2023 European Society of Hypertension Guidelines: what has changed in the management of hypertension in patients with cardiac diseases?

The 2023 Guidelines of the European Society of Hypertensin (ESH) [1] contain several novelties though numerous ground pillars in the management of hypertension remain as before. For example, treatment of masked hypertension may be particularly important if people have hypertension-mediated organ damage such as left ventricular hypertrophy (LVH) or kidney disease expressed as albuminuria or reduced eGFR. Pathophysiology and mechanisms for high blood pressure (BP) are now offered more space in the guidelines [1] including details of the 'Hallmark of Hypertension' which is increased total peripheral vascular resistance with structural changes in pre-capillary arterioles and small arteries. The role of kidneys in regulating fluid and electrolyte balance is emphasised and explains why it remains an important principle that the second or third compound that is prescribed for the treatment of hypertension should always be a diuretic (thiazide or thiazide-like). Patients with severe heart failure with major fluid retention or who have suffered pulmonary oedema, and patients with severe chronic kidney disease (eGFR <30 mL/min/1.73m^2) should as a main rule be treated with a loop-diuretic.

One important novelty of the 2023 ESH Guidelines [1] is the focus on beta-blocker treatment as part of the first-line treatment of hypertension after having revisited the topic [2,3]; importantly, beta-blockers with trial-documented cardioprotective properties in the treatment of heart failure with reduced ejection fraction such as bisoprolol, carvedilol, metoprolol and nebivolol are recommended. This comes in parallel with the very strong recommendation of starting treatment of hypertension with a single-pill combination of two BP lowering compounds in most patients whether it is a blocker of the renin-angiotensin-system (RAS) combined with a calcium-channel blocker or a thiazide/thiazide-like diuretic, or a beta-blocker combined with the same two alternatives. If needed to achieve target BP, the next step should be a single-pill combination of three BP lowering compounds. Various brands combining RAS-blockers, calcium-channel blockers and thiazides/thiazide-like diuretics are available and future development will hopefully also include beta-blockers into triple single-pill drug combinations. Single pill combination treatment is cross-sectionally associated with better drug adherence in common hypertensive patients [4] and a systematic review and meta-analysis of many studies that have started treatment with single pill combinations [5] have shown improved adherence to the treatment and subsequent improved BP control. The use of single pill combinations has also been shown recently to improve persistence and to lower all-cause mortality in hypertension [6].

Target BPs have not changed markedly as 2023 ESH Guidelines [1] recommend that all patient groups including older patients should reach a target of <140/90 mmHg if well tolerated. Further, if possible and well-tolerated, up-titration should take place to achieve target BP <130/80 mmHg in major groups of patients. With triple-compound single-pill combination therapy, ESH guidelines [1] predict that 90% of patients will reach BP target provided excellent drug adherence supported by this form for drug administration. However, the 2023 ESH Guidelines [1] also point to uncertainties regarding target BP in patients with LVH, chronic kidney disease and the older patients as it is still discussed whether a certain perfusion pressure is needed. For example, a post-hoc analysis in patients above the age of 50 years with LVH a publication from the The Valsartan Antihypertensive Long-Term Use Evaluation trial (VALUE) [7], provided observational data suggesting an increased mortality with target systolic BP <130 mmHg in patients with LVH as diagnosed by electrocardiogram (ECG). Similar findings were reported in the Losartan Intervention for Endpoint Reduction in Hypertension (LIFE) study [8], in which all patients had qualified for study participation by having ECG-LVH at baseline.

Care for patients with heart failure and other cardiac diseases has been carefully assessed in the 2023 ESH Guidelines [1]. Though ejection fraction (EF) is still used by many physicians in dividing patients into heart failure patients with reduced EF (HFrEF) and preserved

EF (HFpEF), it appears that in randomised clinical trials of HFpEF patients the same drugs as in HFrEF, but compared to placebo typically on top of the foundational drugs proven in HFrEF, lower hospital admissions and to some degree also mortality whether it is because they lower BP or have a beneficial effect on heart failure per see [9]. The reason is probably that all heart failure patients have reduced systolic function though visualised differently and in HFpEF by missing longitudinal shortening in systole and poor mid-wall systolic function [10]. Thus, the totality of the evidence supports that RAS-blocker or angiotensin receptor neprilysin inhibitor (ARNI), mineralocorticoid receptor antagonist (MRA), beta-blocker and sodium-glucose-cotransporter-2-inhibitor (SGLT2i) are prescribed to all patients with heart failure [1] whereas additional diuretics are given depending on the severity of fluid retention.

BP needs tight monitoring in patients with atrial fibrillation (AF), common in patients with hypertension with and without heart failure, who are under anticoagulant treatment. In these patients, uncontrolled hypertension should be avoided. The SBP target should be 140 mmHg or lower if treatment is well tolerated, while values <120 mmHg should be avoided because of possible U-shaped risk [11]. Also, because many patients with AF have LVH, target SBP should be <140 mmHg and not <130 mmHg, which may increase mortality [7,8]. Oral anticoagulants in patients with marked BP elevation (SBP ≥180 mmHg and/or diastolic BP ≥100 mmHg, i. e. stage III hypertension), may be halted until improved BP control. Finally, most first-line antihypertensive drugs are safe in patients undergoing oral anticoagulation including the use of non-warfarin oral anti-coagulation (NOAC) without a significant risk for clinically relevant drug interactions. The exception applies to the non-dihydropyridine CCB verapamil [12] because verapamil is a moderate inhibitor of the cytochrome P 450 isoenzyme 3A4 and P-glycoprotein and may thereby increase the plasma concentrations of the oral anticoagulants and thus the bleeding risk when used concomitantly [1,12].

There is a linear correlation between BP levels and the risk of death from coronary heart disease (CAD) within a wide range of BP values, starting from 110-115 mmHg SBP and 70-75 mmHg DBP [13]. Hypertension explains approximately 25% of the population-attributable risk of a myocardial infarction. The presence of CAD classifies a patient at a very high cardiovascular risk, even if SBP is <140 mmHg or DBP is <90 mmHg. Many outcome-based randomised controlled trials (RCTs) and their meta-analyses have shown not only that antihypertensive treatment significantly reduces the risk of CAD, although the size of the reduction is less than that of stroke and heart failure, but cardiovascular outcomes are also decreased by BP-lowering interventions in CAD patients [1].

The most common valve disorders of the heart are aortic stenosis, aortic regurgitation (aortic insufficiency) and mitral regurgitation (mitral insufficiency). Detection is usually by auscultation of murmur and subsequent echocardiography. Cardiologists are treating patients with these cardiac conditions when the valve degeneration has developed into a severe condition, and ultimate treatment is open valve surgery or catheter-based valve replacement or repair. Frequently the valve disease is at this stage a component of a heart failure syndrome and patients receive heart failure medications (RAS-blocker or ARNI, beta-blocker, MRA, SGLT2i) as described above. Hypertension is common in patients with cardiac valve disease, but the high BP is usually controlled by the same medications as those used to treat the heart failure syndrome [1].

In conclusion, BP needs careful monitoring in patients with any cardiac disease and treatment should as a main rule be performed with antihypertensive drugs in the category single pill combination with two or three components. However, well-documented drugs like ARNI, beta-blocker, MRA and SGLT2i are not yet included in many single pill combinations and would usually need to be given as add-on medication to patients whose drug adherence must be followed carefully. Target systolic blood pressure is below 140/80 mmHg if well tolerated but a target below 120/70 mmHg should not be actively pursued as there is limited of evidence for this low target.

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