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Hypertension management in chronic kidney disease

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INTRODUCTION

Hypertension (HTN) is one of the most important but still modifiable risk factors for the heart, the brain and the kidney. Indeed, blood pressure (BP) is linearly related to the risk of cardiac events, stroke and kidney disease progression. Volume overload and sodium retention are by far the most important mechanisms, together with sympathetic overactivity, and high renin and aldosterone relative to expanded volumes. HTN is highly prevalent in chronic kidney disease (CKD) and its prevalence increases in parallel with the deterioration of kidney function. In CKD, BP and albuminuria are of paramount importance in disease stratification and monitoring. Serum creatinine, estimated glomerular filtration rate (eGFR) and urine albumin-to-creatinine ratio should be documented in all hypertensive patients and if CKD is diagnosed, repeated at least annually.

BP ASSESSMENT AND BP TARGETS

The 2012 KDIGO Guidelines formally recommend that the diagnosis and treatment of HTN have to be made by office BP measurements. Patients are stratified according to the presence/absence of diabetes and albuminuria. In non-diabetic patients without albuminuria, BP targets are <140/90 mmHg. In non-diabetic CKD patients with mild microalbuminuria, the BP target should be aimed at <130/80 mmHg. The recommendation is that adults with diabetes and CKD with urine albumin excretion <30 mg/24 h whose office BP is consistently >140 mmHg systolic or >90 mmHg diastolic be treated with BP-lowering drugs to maintain a BP that is consistently ≤140 mmHg systolic and ≤90 mmHg diastolic. In addition to that, it is suggested that adults with diabetes and CKD with urine albumin excretion >30 mg/ 24 h whose office BP is consistently >130 mmHg systolic or >80 mmHg diastolic be treated with BP-lowering drugs to maintain a BP that is consistently ≤130 mmHg systolic and ≤80 mmHg diastolic. Home BP monitoring is an alternative strategy that is less expensive and more affordable worldwide than ambulatory BP monitoring (ABPM). The 2017 American College of Cardiology (ACC) Guidelines suggest out-of-office BP measurement to confirm the diagnosis of HTN and for monitoring BP-lowering agents in all patients by validated home BP devices. Furthermore, ACC guidelines also indicate that there is a good relationship between clinic and out-of-clinic BP measurements, suggesting that a clinic BP of 140/90 mmHg corresponds to a home BP value of 135/85 mmHg and to daytime and nocturnal ABPM values of 135/85 and 120/70 mmHg, respectively. BP targets are simplified in the National Kidney Foundation Clinical Practice Guidelines, which recommend a BP goal of <130 mmHg systolic and <80 mmHg diastolic for all CKD patients.

TREATMENT OPTIONS: NON-PHARMACOLOGICAL AND PHARMACOLOGICAL

Non-pharmacological treatment in hypertensive CKD patients is first of all a reduction of salt in the diet. Salt has been proven to be of paramount importance for BP control and for proteinuria [1] and shows great promise as a modifiable risk factor for reducing the risks of cardiovascular (CV) disease and CKD progression [2].

Another non-pharmacological line of intervention is body weight reduction in obese hypertensive patients. The beneficial effects of weight loss approaches on proteinuria and HTN in the CKD population have been widely documented, and the National Kidney Foundation has already recommended weight reduction for diabetic patients with CKD Stages 1–4 [3]. Bolignano and Zoccali [4] demonstrated weight loss to be effective in reducing BP and proteinuria with no further decrease in GFR.

Another non-pharmacological approach includes physical activity, which was proven to significantly decrease systolic BP in a meta-analysis in patients with Stages 2–5 CKD [5].

Pharmacological treatment in hypertensive CKD patients aims at reducing BP and providing reno-cardioprotection [6]. Multidrug regimens are usually necessary to achieve BP goals in patients with CKD [6, 7].

Angiotensin-converting enzyme (ACE) inhibitors [or an angiotensin receptor blockers (ARB), in the case of ACE inhibitor intolerance] are the most preferred treatment for hypertensive CKD patients. The use of ACE inhibitors has been recommended for all patients with Stage 3 CKD or higher. ACE inhibitors or ARBs are also suggested for patients with Stages 1–2 CKD with significant albuminuria. On the other hand, combination therapy with both an ACE inhibitor and an ARB is no

Table 1. Clinical considerations and strategies for the treatment of HTN in CKD patients and recommendations

Clinical considerations		
Albuminuria reduction has also been considered as a therapeutic target. However, whether reducing albuminuria *per se* is a proxy for cardiovascular disease prevention remains unclear.		
CKD patients should receive lifestyle advice, especially sodium restriction.		
Loop diuretics should replace thiazide diuretics when the eGFR is <30 mL/min/1.73 m^2.		
Because BP lowering reduces renal perfusion pressure, it is expected and non-unusual for eGFR to be reduced by 10–20% in patients treated for HTN. Careful monitoring of blood electrolytes and eGFR is essential.		
Recommendations	**Class**	**Level**
In patients with diabetic or non-diabetic CKD, it is recommended that an office BP of ≥140/90 mmHg be treated with lifestyle advice and BP-lowering medication.	I	A
In patients with diabetic or non-diabetic CKD:		
It is recommended lower SBP to a range of 130 to <140 mmHg.	I	A
Individualized treatment should be considered according to its tolerability and impact on renal function and electrolytes.	IIa	C
RAAS blockers are more effective at reducing albuminuria than other antihypertensive agents and are recommended as part of the treatment strategy in hypertensive patients in the presence of microalbuminuria or proteinuria.	I	A
A combination of a RAS blocker with a CCB or a diuretic is recommended as initial therapy.	I	A
A combination of two RAS blockers is not recommended.	III	A

Derived from 2018 ESC/ESH Guidelines for the management of arterial HTN.

longer advised in those with CKD [8]. Current guidelines suggest that a rise in serum creatinine of up to 30% with subsequent stabilization should be accepted following initiation of Renin-Angiotensin-Aldosterone System (RAAS) blockade, as this is likely to confer longer-term renoprotection [9]. The use of RAAS blockade in those with advanced CKD (eGFR <30 mL/min/1.73 m_2) is uncertain as this population has been largely excluded from major randomized trials.

Diuretics are frequently used as part of combination drug therapy in CKD and offer antihypertensive and cardioprotective effects. In non-proteinuric CKD, monotherapy with a thiazide or a thiazide-like diuretic may have a role and should be considered as a potential for first-line therapy in CKD patients with an eGFR >60 mL/min [9]. Loop diuretics (i.e. furosemide) are valuable, although higher doses are often required in those with a lower eGFR.

Mineralocorticoid receptor antagonists (blockers; such as spironolactone) effectively reduce BP in CKD but run the risk of exacerbating hyperkalaemia.

Calcium channel antagonists (blockers) both dihydropyridine (i.e. amlodipine) and non-dihydropyridine (i.e. verapamil) calcium-channel blockers (CCBs) are useful in the management of HTN in CKD patients. Dihydropyridine CCBs can be used as first-line therapy in non-proteinuric CKD, either alone or in combination. The addition of a dihydropyridine CCB to proteinuric patients with established RAAS blockade improves BP control without worsening proteinuria. Although generally well-tolerated, CCBs have the potential to worsen peripheral oedema, something that can be particularly troublesome for those with CKD.

β-Blockers (β-adrenoceptor antagonists) effectively reduce BP in CKD due to their effect on the sympathetic nervous system. The cardioprotective benefits of these drugs are well established even in CKD patients.

Peripherally acting α-adrenoceptor antagonists (i.e. doxazosin) are often used as part of combination therapy for the management of HTN in CKD but they should not be considered for first-line therapy. In patients with CKD and HTN, taking at least one antihypertensive medication at bedtime, improves control of BP and reduces CV risk [10]. A summary of clinical considerations and treatment strategies of HTN in CKD patients is given in Table 1.

CONFLICT OF INTEREST STATEMENT

None declared.

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