Review Article

Current Trends in Hypertension: Takeaways from the 2021 KDIGO Guidelines for the Management of Blood Pressure in Chronic Kidney Disease

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Abstract

The new 2021 Kidney Disease Improving Global Outcomes (KDIGO) guidelines on the management of blood pressure in chronic kidney disease (CKD) patients were published in March 2021 in Kidney International. The full issue exceeds 80 pages. The author of this article aims to provide a succinate summary of the main points of the guidelines with special emphasis on the changes introduced since the previous 2012 guidelines. These KDIGO guidelines are evidence-based, and they are graded accordingly. As with any recent hypertension guidelines, they incorporate and emphasize the results of The Systolic Blood Pressure Intervention Trial (SPRINT) published in 2015.

Keywords: Hypertension, CKD, KDIGO guidelines, SPRINT

1. Introduction

1.1 The Systolic Blood Pressure Intervention Trial (SPRINT)

SPRINT was published in 2015 [1, 2]. It is a landmark study in hypertension. SPRINT enrolled 9361 subjects. It was a randomized, multicenter, and controlled trial. The enrollees were 50 years or older

with systolic blood pressure (SBP) above 130 mm Hg and one of the following conditions: CKD (estimated glomerular filtration rate [eGFR] 20-59 ml/min/1.73 m^2), history of cardiovascular disease (CVD), intermediate to high risk for CVD other than cerebrovascular accident (CVA), or age over 75 years. The standard treatment target was SBP< 140 mm Hg, while the intensive treatment target was SBP < 120 mm Hg. In the group randomized to the lower SBP goal of (< 120 mm Hg), the primary combined cardiovascular endpoints decreased by 25%, while mortality was reduced by 27%.

CKD defined as eGFR 20-59 ml/min/1.73 m^2 was present in 28% of SPRINT subjects. Based on SPRINT inclusion and exclusion criteria, none of the subjects had polycystic kidney disease or proteinuria ≥ 1 g/day. In the SPRINT-CKD cohort, there was no difference between the standard and intensive treatment groups with regard to serious adverse events or end-stage renal disease (ESRD). The intensive treatment group had a lower mortality rate [3]. The higher risk of ≥ 30% decline in eGFR in the intensive treatment group was credited to the hemodynamic effect of intensive blood pressure (BP) lowering. The decline was ameliorated after the initial 6 months of intensive BP therapy.

1.2 Rating of recommendations

The strength of each recommendation in the guidelines is indicated as Level 1 (strong, the authors recommend), or Level 2 (weak, the authors suggest), and the quality of the supporting evidence is shown as A (high), B (moderate), C (low), or D (very low) [4].

1.3 Chronic kidney disease (CKD) categories

Based on GFR in ml/min/1.73 m^2, CKD is divided into five categories or stages: G1 (GFR ≥ 90), G2 (60-89), G3a (45-59), G3b (30-44), G4 (15-29), and G5 (<15) [5].

1.4 Persistent albuminuria categories

A1 (<30 mg albumin /g creatinine, or < 3 mg albumin/mmol creatinine), A2 (30-300 mg/g, or 3-30 mg/mmol), and A3 (>300 mg/g, or >30 mg/mmol) [5].

2. Summary of Guidelines

2.1 Blood pressure measurement

Standardized office BP measurement rather than routine BP measurement is recommended for high BP management in adults. An Oscillometric BP device may be preferable to a manual one. The former may be used in atrial fibrillation patients. An automated office BP device whether attended or unattended is preferred. All the above recommendations are rated (1B). Ambulatory (ABPM) and home BP (HBPM) monitoring are complementary to standardized office BP measurement (2B) [6]. HBPM should not solely guide BP management. It is worth mentioning that SPRINT utilized a fully automated oscillometric BP device. BP readings were attended by staff at some but not all of the study centers [1]. This automated approach was implemented to reduce errors in BP measurements and possibly reduce white coat effect. Ambulatory self BP monitoring should only be done via a certified device. The American Medical Association published a list of validated devices in the United States after conducting an independent review process. It can be found online at: https://www.validatebp.org.

Standardized office BP measurement should be done in a quiet room, the patient is seated, and the back is supported while the feet are flat on the floor **[6]**. The arm is bare and resting at the same level of the device. No talking by the patient or the observer is allowed. The patient should not have smoked,

consumed caffeine, or exercised for 30 minutes. The patient should relax with an empty bladder for at least five minutes prior to BP measurement. Cuff size should be appropriate for the arm, and the device should be calibrated periodically. It is important to know that BP measurements using a standardized office BP measurement protocol may yield different results compared to routine office BP measurements. The relationship between the two measurements is variable and a correction factor to convert one to the other does not exist.

2.2 Lifestyle interventions for non-dialysis CKD patients

The guidelines recommend sodium intake <2 g per day (<90 mEq or 90 mmol/day), or <5 g of sodium chloride (NaCl) per day (2C) [6]. Utilization of diets that are high in potassium such as [The Dietary Approaches to Stop Hypertension (DASH)] or potassium-containing salt substitutes is not appropriate for CKD patients prone to hyperkalemia such as those with diabetic kidney disease and hyporeninemic hypoaldosteronism. Depending on the fitness level and cardiovascular tolerance of the patient, a moderately intense physical activity of a minimum of 150 minutes per week is recommended (2C).

2.3 Blood pressure targets

The 2012 guidelines recommended a target BP (<130-140/80-90) mm Hg depending on the specific CKD population [7]. The updated 2021 guidelines recommend a target systolic blood pressure SBP of <120 mm Hg using standardized office BP measurement (2B) [4]. This target reduces major cardiovascular events and all-cause mortality in CKD patients. It is unclear whether it impacts kidney disease progression. This lower target is based on the results of SPRINT [3]. The benefits of this intensive BP lowering (SBP <120 mm Hg) is less certain in diabetics with CKD, patients with stage 5 CKD, and those with A3 albuminuria (>300 mg/g, or >30 mg/mmol). This conclusion is based on the results of previous clinical trials including ACCORD, MDRD, AASK, and REIN-2 [8-11]. A higher target may be considered in patients with postural hypotension or limited longevity.

2.4 Choice of antihypertensive drugs

Inhibitors of the renin-angiotensin-system (RASi) including (angiotensin converting enzyme inhibitor [ACEi] or angiotensin II receptor blocker [ARB]) are recommended for non-diabetics with high BP, CKD (G1, G2, G3, and G4) and A3 albuminuria (>300 mg/g, or >30 mg/mmol) [1B] and suggested in case of A2 albuminuria (30-300 mg/g, or 3-30 mg/mmol) [1C] [11]. The same recommendation applies to diabetics with A2 or A3 albuminuria with a (1B) rating [12, 13]. Several practical points are emphasized by the authors of the guidelines regarding the choice of antihypertensive drugs. RASi may be used for managing hypertensive CKD patients without albuminuria. This applies to both diabetic and non-diabetic patients. Since clinical trials with RASi utilized the highest tolerated approved doses, the same approach should be used to maximize the benefit of these medications. BP and a chemistry panel including creatinine and potassium should be checked within 2-4 weeks of treatment initiation of RASi. There is no indication to discontinue treatment with RASi unless creatinine rises by more than 30% within 4 weeks of treatment initiation or dose escalation. Measures to mitigate hyperkalemia should be implemented (low potassium diet, potassium binders), rather than dose reduction or discontinuation [14, 15]. A retrospective review of a large database of electronic health records involving over 200,000 patients, showed that RASi discontinuation or dose reduction is associated with increased

mortality [16]. On the other hand, RASi discontinuation or dose reduction maybe considered in hyperkalemia unresponsive to medical treatment, symptomatic hypotension, or patients with stage 5 CKD (G5, GFR < 15 ml/min/1.73 m^2) to reduce uremic symptoms. Mineralocorticoid receptor antagonists such as spironolactone are effective in CKD patients with resistant hypertension; however, hyperkalemia and a reversible decline in renal function are limiting factors especially in patients with advanced CKD [17].

2.5 Dual therapy with RASi

The use of any combination of ACEi, ARB, and direct renin inhibitors is not recommended in patients with CKD, with or without diabetes (1B) [18].

2.6 Kidney transplant recipients

BP target in adult kidney transplant recipients is <130 mm Hg systolic and <80 mm Hg diastolic. This is the same recommendation from the previous 2012 guidelines [7]. There are no published randomized clinical trials concerning different BP targets and subsequent clinical outcomes in kidney transplant recipients. In this population, dihydropyridine calcium channel blockers (CCB) or ARB are first-line antihypertensive agents (1C) [19, 20].

2.7 Children with CKD

Ambulatory BP monitoring (ABPM) should be done in children with CKD to determine 24-hour mean arterial pressure (MAP). MAP should be lowered to ≤ 50^{th} percentile for height, age, and sex of the child (2C) [21]. ABPM is suggested annually for BP monitoring in children with CKD. Otherwise, regular monitoring with standardized auscultatory office BP monitoring is done every 3-6 months. If ABPM is not available, standardized manual auscultatory office BP should be lowered to achieve SBP <90^{th} percentile for height, age, and sex of the child. ACEi or ARB are first-line therapy, but they should be avoided in pregnancy.

3. Conclusion

The new 2021 KDIGO guidelines on the management of blood pressure in chronic kidney disease (CKD) patients update the 2012 guidelines. They recommend a target systolic blood pressure SBP of <120 mm Hg and emphasize the importance of using standardized office BP measurement. RASi are recommended as first line agents. Any combination of ACEi, ARB, and direct renin inhibitors should be avoided. Pending further data, adult kidney transplant receipts should be treated to a BP target of (<130/<80) mm Hg.

Conflict of Interest

None

References

1. The SPRINT Research Group. A Randomized Trial of Intensive versus Standard Blood-Pressure Control. New England Journal of Medicine 373 (2015): 2103-2116.
2. The SPRINT Research Group. Final Report of a Trial of Intensive versus Standard Blood-Pressure Control. New England Journal of Medicine 384 (2021): 1921-1930.
3. Cheung AK, Rahman M, Reboussin DM, et al. Effects of intensive BP control in CKD. Journal of the American Society of Nephrology 28 (2017): 2812-2823.
4. Kidney Disease: Improving Global Outcomes (KDIGO) Blood Pressure Work Group. KDIGO 2021 Clinical Practice Guideline for the Management of Blood Pressure in Chronic Kidney Disease. Kidney International 99 (2021): 1-87.

5. Group KDIGO (KDIGO) CW. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney International 3 (2013): 1-150.
6. Whelton P, Carey R, Aronow W, 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: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Pr. Hypertension 71 (2018): e13-e115.
7. Kidney Disease: Improving Global Outcomes (KDIGO) Blood Pressure Work Group. KDIGO Clinical Practice Guideline for the Management of Blood Pressure in Chronic Kidney Disease. Kidney Int 2 (2012): 337-414.
8. Group TAS. Effects of Intensive Blood-Pressure Control in Type 2 Diabetes Mellitus. New England Journal of Medicine 362 (2010): 1575-1585.
9. Group. M of D in RDS. The effects of dietary protein restriction and blood-pressure control on the progression of chronic renal disease. New England Journal of Medicine 330 (1994): 877-884.
10. Wright Jr JT, Bakris G, Greene T, et al. Effect of blood pressure lowering and antihypertensive drug class on progression of hypertensive kidney disease: results from the AASK trial. JAMA - Journal of the American Medical Association 288 (2002): 2421-2431.
11. Ruggenenti P, Perna A, Loriga G, et al. Blood-pressure control for renoprotection in patients with non-diabetic chronic renal disease (REIN-2): multicentre, randomised controlled trial. Lancet 365 (2005): 939-946.
12. Brenner B, Cooper M, de Zeeuw D, et al. Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. New England Journal of Medicine 345 (2001): 861-869.
13. Lewis E, Hunsicker L, Clarke W, et al. Renoprotective effect of the angiotensin-receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes. New England Journal of Medicine 345 (2001): 851-860.
14. Tinawi M. Potassium Binders. Arch Intern Med Res 3 (2020): 141-145.
15. Palmer BF. Potassium Binders for Hyperkalemia in Chronic Kidney Diseased-Diet, Renin-Angiotensin-Aldosterone System Inhibitor Therapy, and Hemodialysis. Mayo Clin Proc 95 (2020): 339-354.
16. Epstein M, Reaven N, Funk S, et al. Evaluation of the treatment gap between clinical guidelines and the utilization of renin-angiotensin-aldosterone system inhibitors. Am J Manag Care 21 (2015): S212-S220.
17. Carey RM, Calhoun DA, Bakris GL, et al. Resistant hypertension: Detection, evaluation, and management a scientific statement from the American Heart Association. Hypertension 72 (2018): e53-e90.
18. Fried L, Emanuele N, Zhang J, et al. Combined Angiotensin Inhibition for the Treatment of Diabetic Nephropathy. New England Journal of Medicine 369 (2013): 1892-1903.
19. Ibrahim H, Jackson S, Connaire J, et al. Angiotensin II blockade in kidney transplant recipients. J Am Soc Nephrol 24 (2013): 320-327.

20. van Riemsdijk I, Mulder P, de Fijter JW, et al. Addition of isradipine (Lomir) results in a better renal function after kidney transplantation: a double-blind, randomized, placebo-controlled, multi-center study. Transplantation 15 (2000): 122-126.

21. Group ET. Strict blood-pressure control and progression of renal failure in children. New England Journal of Medicine 361 (2009): 1639-1650.