Target of blood pressure in CKD

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Introduction

- Around 850 million people worldwide have CKD and >80% of them have hypertension
- High blood pressure is an important risk factor for CKD and its progression and CVD
- Mortality from CKD is projected to become the fifth leading cause of death by 2040.
- Among many question concerning the optimal management of high BP in CKD, setting targets for BP control is crucial

Causes of hypertension in CKD

- Renin – angiotensin- aldosterone system
- Sympathetic nervous system
- Endothelial dysfunction
- Insulin resistance
- Hyperparathyroidism
- Reduce nephron mass

The main point of discussion

- History of the recommendation of BP targets
- Major guidelines on BP targets for CKD
- Challenges
- Treatment and key points

Establishment of target of BP 140/90

- VA Cooperative Study in: 143 male DBP 115-129
- 2nd VA Cooperative Study; 360 patients: DBP 90 - 114
- Clinical trail 1970s and 1980 established BP <140/90 target of BP

Intensive BP LOWERING in DM and CKD

- Hypertension optimal treatment(HOT)
  - 18790 patients, age 50-80, DBP 100-115
  - Target ≤90, ≤85, ≤80
  - No difference in CV events
  - In 1501 DM major CV events in DBP ≤80 was lower than ≤90

- MDRD :840 CKD non DM
  - MEAN BP 92 vs 107
  - Proteinuria>1g/d intensive BP control slow decline in GFR

*2003 JNC 7 recommended a treatment target BP of 140/90 and BP goal <130/80 for DM and CKD

Revision of target BP to 140/90 for all hypertension regardless of associated conditions

- Accord Study in 2010 :benefits of BP control in DM
  - 4733 patients(BP <120 vs <140) follow up 4.7 yr
  - Not reduce fetal and non fetal CV reducing rate of stroke
  - For CKD the evidence for benefits was unclear
- REINS2 Study
- AASKD
  - Intensive BP control failed to show benefits in slowing progression of KD
- Based these ,ESH/ESC(2013) & 2014 JNC 8 recommended target <140/90
- DBP 85 for DM (European guide)

Back to 130/80: intensive BP treatment for all hypertensive

- SPRINT:2015
  - 9361 patients without DM,age > 50 relatively high risk . AOBP was used
  - BP <120 vs <140
  - Trial was stopped in 3.26 yr due to significant CV risk reduction
- Subsequent meta-analysis of BP lowering trials demonstrated benefits especially at high CV risk
- ACC/AHA
- ESH/ESC

*Intensive BP lowering may be beneficial but too much reduction 120/70 ?

Current recommendation

- ESC guideline:
- KDIGO :

From KDIGO 2012 to KDIGO 2021

- KD1GO 2012
  - BP < 140/90 in CKD non diabetic, normoalbuminuric
  - BP < 130/80 in CKD with albuminuria and transplant patients
  - No recommendation for dialysis patients
- KD1GO 2021
  - BP < 120/80 in CKD when tolerated
  - Provide guide how to measured office BP

From ESC/ESH 2018 to 2021

- 2018 ESC/ESH
  - Therapy for patients with CKD> 80 yr started in BP ≥ 160/90
  - Threshold in younger was ≥ 140/90
  - Target was the same for adult CKD of all ages 130-139 / 70-79
  - Younger with no CKD and diabetes 120-129
- ESC 2021
  - Decrease differential SBP thresholds at which to initiate therapy based on age
  - Still recommends a higher SBP target 130-130 in adults with CKD at any age
  - Younger people in the general population or I DM 120-130 if <70 and 130-139 if ≥ 70

Key question regarding the discrepancy in SBP targets between KDIGO and ESC 2021

- Do the new guidelines cite different evidence of their BP targets in CKD
- Do they recommend different methods to measure office BP
- Does the guideline ESC 2021 acknowledge the earlier guidelines in the same year (KDIGO)
- Does the ESC explain why its BP targets differ from KDIGO

- The KDIGO target systolic BP <120 mmHg target is based on CKD subgroup analysis of a single randomized controlled trial (SPRINT).
- The target is not generalisable as SPRINT excluded people with diabetes (also not supported by ACCORD trial), ADPKD, GN on immunosuppression, proteinuria >1 g/day and CKD stages 4 (very few patients included) & 5.
- The target refers to standardized BP and not to routine office BP.
- Standardized BP measurement is important for initiating and monitoring treatment of hypertension, but is challenging to implement outside specialist hypertension and research clinics.
- The target will increase the risk of adverse events in the multi-morbid, frail and elderly CKD population, especially if applied to routine BP measurement.
- The target will be difficult to achieve in the majority of CKD patients based on current evidence.
- The target systolic BP <120 mmHg recommended by KDIGO is an outlier among the contemporary international hypertension guidelines and will perplex clinicians.

International guideline target BP

- JNC 7 :
  - General BP goal is < 140/90
  - Goal of < 130/80 for DM or CKD
- JNC 8:
  - Less than 140/90 in 18-59 yr without comorbidities
  - In patients 60 or older with DM or CKD or both goal is < 140/90
  - 60 or older without DM or CKD < 150/90
- ACC/AHA 2017: target of < 130/90
- ESC/ESH: recommends SBP 130-139
  - National institutes for health and care: < 140/90 in CKD and ACR<70
  - And SBP 120-129 for CKD and ACR >70 mg/mol
- KDIGO (2021): recommends SBP<120

Table 2. Criteria for Hypertension Based on Office-, Ambulatory (ABPM)-, and Home Blood Pressure (HBPM) Measurement

	SBP/DBP, mm Hg
Office BP	≥140 and/or ≥90
ABPM	
24-h average	≥130 and/or ≥80
Day time (or awake) average	≥135 and/or ≥85
Night time (or asleep) average	≥120 and/or ≥70
HBPM	≥135 and/or ≥85

	Routine/conventional office blood pressure (manual measurement with stethoscope or oscillometric device)*	Unattended AOBPM, daytime ABPM, or home blood pressure ¶
Higher-risk population △		
▪ Known ASCVD ◇ ▪ Heart failure ▪ Diabetes mellitus ▪ Chronic kidney disease ▪ Age ≥65 years § ▪ Calculated 10-year risk of ASCVD event ≥10% ¥	125 to 130/<80	120 to 125/<80
Lower-risk ‡		
▪ None of the above risk factors	130 to 139/<90	125 to 135/<90

Target BP in CKD

- Intensive BP control compered with conventional During trial
- Intensive BP control mean ≤ 92 (e.g BP ≤ 120/85) compered with usual control a mean BP ≤ 107 (e.g. BP ≤140/90) in extended follow up
- SPRINT
  - Non DM patients at a high risk of CVE BP < 120 compared with < 140
  - results: lower rates of CV events and all causes of mortality
  - Of the 9361 cases 2646 had an eGFR <60 and 1723 had a urine ACR of ≥ 30 risk reduction was similar

More intensive VS less intensive

- Reduce risk of ESRD in patients with CKD and proteinuria
- May reduce mortality in patients with CKD
- Mortality benefit is most evident when patients are followed long term

* The evidence four main studies that BP target in CKD patients

(ACCORD, SPS3, SPRINT, STEP)

Trial, year	Design	Size	Sample	Mean age, years	SBP/DBP, mm Hg			Results	
					Baseline	SBP targets	Achieved	Primary outcome	Primary outcome results
ACCORD, 2010[17]	2-by-2 factorial RCT (BP and glycemic interventions)	4,733	Adult diabetics at high risk for CVD	62	139/76	<120 and <140	119/64 and 133/70	CVD composite	No significant treatment difference, using prespecified (factorial) analysis. Nominal SPRINT-like benefit for intensive BP lowering in normoglysemic subgroup.
SPS3, 2013[18]	2-by-2 factorial RCT (BP and antiplatelet interventions)	3,020	Adults with recent lacunar stroke	63	143/79	<130 and 130–149	127/— and 138/—	Recurrent stroke	Nonsignificant ($P = 0.08$) lower event rate in intensively treated group.
SPRINT, 2015[19] and 2021[20]	2-Arm parallel RCT	9,361	Adults with high BP and high risk of CVD. No diabetics or stroke survivors. Strong representation of older adults and patients with CKD	68	140/78	<120 and <140	119/— and 136/— (median after 6 months)	CVD composite	Significant 27% benefit for intensive treatment group.
STEP, 2021[21]	2-Arm parallel RCT	9,624	Adults 60–80 years, with high BP. High CVD risk cohort	66	146/82	110–129 and 130–149		CVD composite	Significant 26% benefit for intensively treated group.

Abbreviations: BP, blood pressure; CKD, chronic kidney disease; CVD, cardiovascular disease; DBP, diastolic blood pressure; RCT, randomized controlled trial; SBP, systolic blood pressure. (i) Accord Study Group.[17] (ii) SPRINT Research Group.[20]

Safety of the low BP target

- Postural hypertension
- Recurrent falls and fracturs
- Stroke in those with lower carotid reserve
- Rapid decline in eGFR in RVD
- Potential hazards of too low DBP
- Polypharmacy

Polypharmacy

- Use of ≥ 5 pharmacological agents
- Common in elderly and multimorbid individual
- It is associated with adverse drug reaction ,drug interaction and nonadherence
- Higher direct and indirect health care cost

Challenges of implementation of standardized BP measurements

- Requires significant resources staff training clinic space validated BP devices
- Most of the early stage of CKD are cared for in primary cared
- In developing country implementation standardized BP measurement is more challenging
- Possibility of reconfiguration of outpatients service into virtual clinics.

Hypertension management in CKD

- Renin-Angiotensin-Aldosterone system inhibitors: Finerenone
- New classes
  - Sacubitril-valsartan
  - SGLT2 inhibitors

Key points

- Lowering BP to <120/80 increase the risk of other serious adverse events
- Standardized BP measurement increase the burden on patients and resources
- Evaluation home or ambulatory BP measurement as a treatment target are needed

*Targeting office BP <130/80 using an appropriate office BP

measurement can be an option and is recommended for most adults

al high risk of CVD

- The pressure and degree of albuminuria would be considered to determine individual BP targets