



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

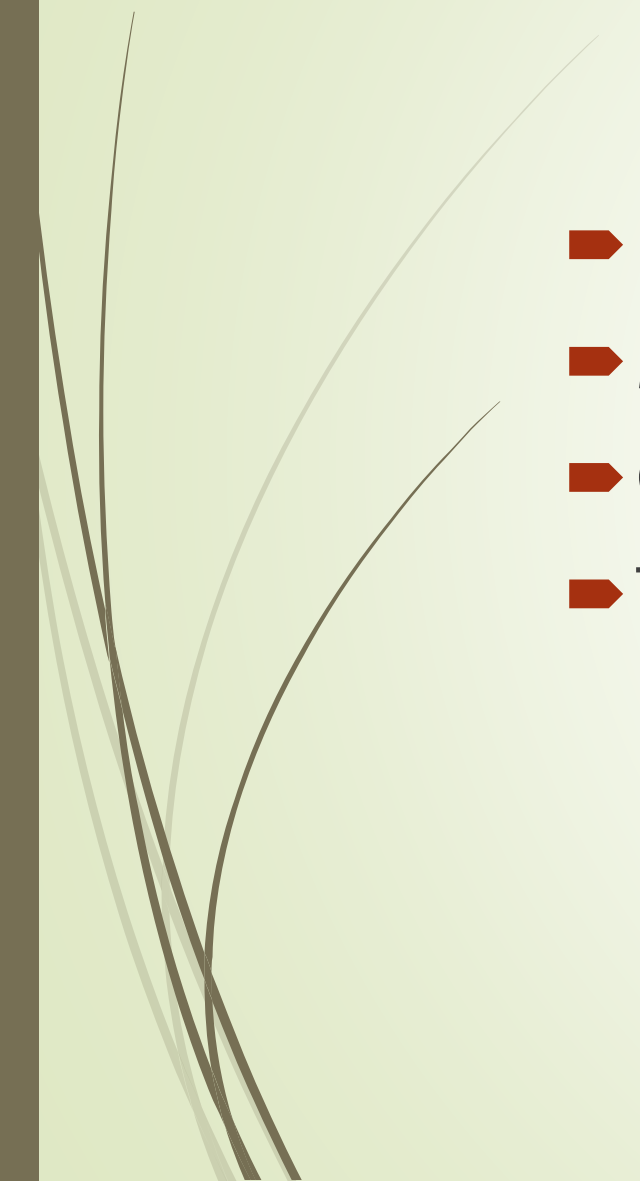


Causes of hypertension in CKD

- 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
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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 $> 1\text{g/d}$ 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

➤ KDIGO 2012

- BP < 140/90 in CKD non diabetic, normoalbuminuric
- BP < 130/80 in CKD with albuminuria and transplant patients
- No recommendation for dialysis patients

➤ KDIGO 2021

- BP < 120/80 in CKD when tolerated
- Provide guide how to measure office BP




From ESC/ESH 2018 to 2021

- 2018 ESC/ESH
 - Therapy for patients with CKD > 80 yr started in BP \geq 160/90
 - Threshold in younger was \geq 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 \geq 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

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- 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[△]		
<ul style="list-style-type: none"> ■ Known ASCVD[◇] ■ Heart failure ■ Diabetes mellitus ■ Chronic kidney disease ■ Age ≥ 65 years[§] ■ Calculated 10-year risk of ASCVD event $\geq 10\%$[¥] 	125 to 130/ < 80	120 to 125/ < 80
Lower-risk[‡]		
<ul style="list-style-type: none"> ■ None of the above risk factors 	130 to 139/ < 90	125 to 135/ < 90



Target BP in CKD

- Intensive BP control compared with conventional During trial
- Intensive BP control mean ≤ 92 (e.g BP $\leq 120/85$) compared with usual control a mean BP ≤ 107 (e.g. BP $\leq 140/90$) 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

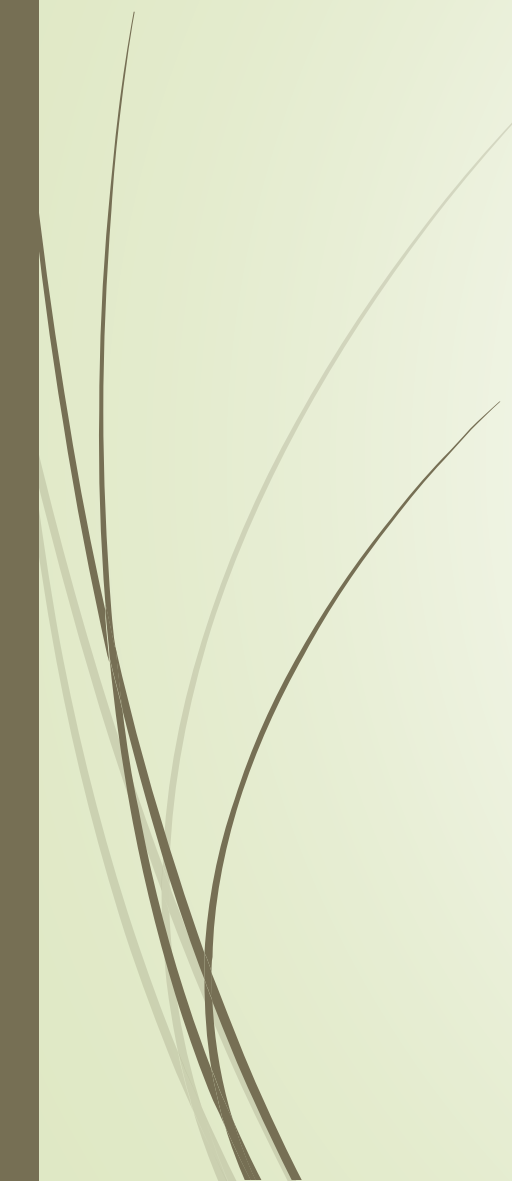
* The evidence four main studies that BP target in CKD patients
(ACCORD, SPS3, SPRINT, STEP)

Trial, year	Design	Size	Sample	Mean age, years	SBP/DBP, mm Hg			Primary outcome	Results
					Baseline	SBP targets	Achieved		
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

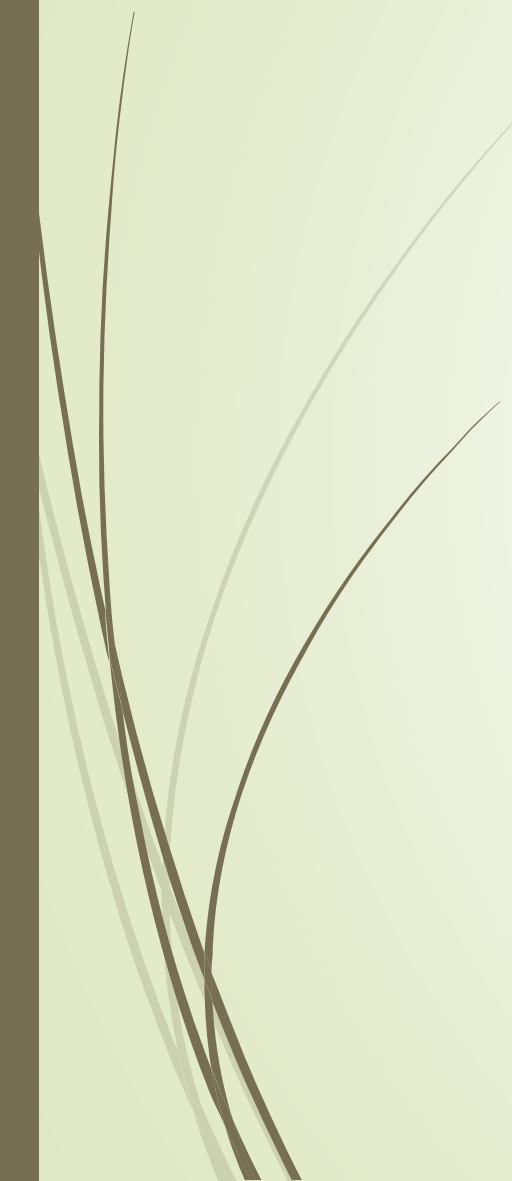



Safety of the low BP target

- Postural hypertension
 - Recurrent falls and fractures
 - Stroke in those with lower carotid reserve
 - Rapid decline in eGFR in RVD
 - Potential hazards of too low DBP
 - Polypharmacy
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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
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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 care
- 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 at high risk of CVD
- ▶ The pressure and degree of albuminuria would be considered to determine individual BP targets