Hypertension and Chronic Kidney Disease...

An Unhappy Marriage



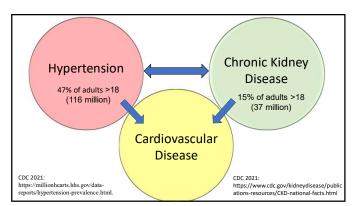
Harvey A. Feldman, MD, FACP, FASN Professor, Physician Assistant Program Nova Southeastern University, Ft. Lauderdale, FL

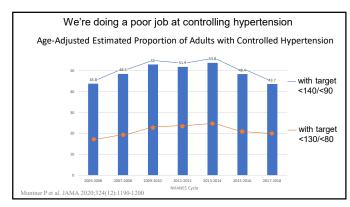
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Outline

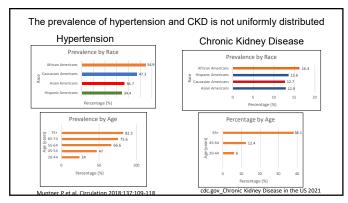
- Epidemiology and the bidirectional pathophysiologic relationships between hypertension and CKD
- · Hypertension phenotypes prevalent in CKD
- Key points in evaluation of hypertension in CKD
- Comorbidities associated with hypertension in CKD
- New 2021 KDIGO hypertension guideline for CKD Comparison with the 2017 ACC/AHA hypertension guideline

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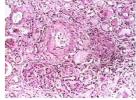


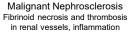
We're doing a poor job at diagnosing and managing CKD			
	10 adults with CKD know they have CKD		
2 in 5 adults with severe CKD don't know they have CKD	CDC 2021: https://www.cdc.gov/kidneydisease/ publications-resources/CKD-national- facts.html		
Cross-sectional study of patients in 466 primary care practices across the U.S.:			
Only 12.1% of the 5,036 patients with T2DM and CKD were diagnosed!			
CKD Stage	Percent diagnosed		
1 (Kidney damage with GFR >90 mL/min/1.73 m ²)	1.1		
2 (Mild reduction in GFR, 60-89 mL/min/1.73 m ²)	4.9		
3 (Moderate reduction in GFR, 30-59 mL/min/1.73m ²)	18.0		
4 (Severe reduction in GFR, 15-29 mL/min/1.73m ²)	52.9		
5 End-stage kidney disease, GFR <15 mL/min/1.73m ²)	58.8		
Szczech LA. PLoS One 2014;9(11):e110535			



Does Hypertension **CAUSE** Kidney Disease?

Hypertensive Crisis







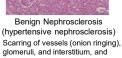
- Clinically.....
 - Acute kidney injury
 - Hematuria
 - Proteinuria
 - Microangiopathic hemolytic anemia (schistocytes)

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Does Hypertension **CAUSE** Kidney Disease?

Chronic Hypertension





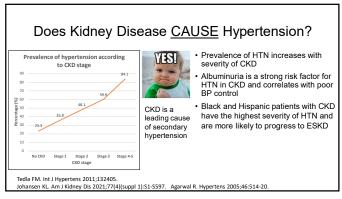
tubular atrophy and dilation

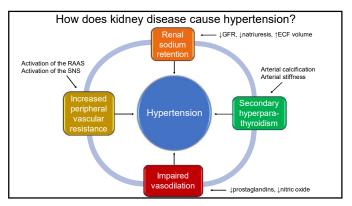


- Clinically.....
 - Slowly rising creatinine (over many years)
 - Little or no proteinuria
 - · Accounts for 25% of ESKD
- Problems..... · HTN is so common, a small percentage of patients at risk of ESKD = large number
- (hypertensive nephrosclerosis) Kidney biopsies are rarely done to r/o other dxs
- Scarring of vessels (onion ringing), African Americans with ESKD attributed to HTN may have ESKD due to the APOL1 gene variant
 - Pathology and clinical phenotype are nonspecific

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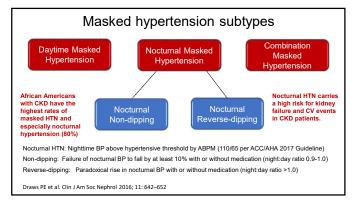
How does hypertension cause kidney disease? Hypertension Impaired autoregulation of renal blood flow and filtration Ischemia Model 4 ➤ Hyperfiltration Arterial and arteriolar Glomerular Model narrowing hypertension Glomerular Decreased RBF and GFR hyperfiltration Renal ischemia Glomerular scarring, tubulointerstitial fibrosis and scarring Nephrosclerosis



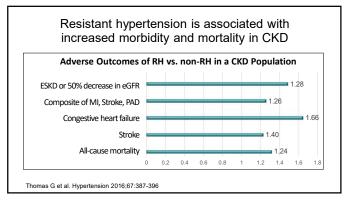


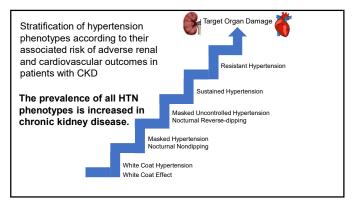
Hypertension Phenotypes based on office and home or ambulatory BP			
Untreated patients		Treated patients	
Normal office BP and Normal home or ABPM Sustained normotension	High office BP but Normal home or ABPM White coat hypertension	Normal office BP and Normal home or ABPM True BP control	High office BP but Normal home or ABPM White coat effect (white coat uncontrolled HTN)
High office BP and High home or ABPM Sustained hypertension	Normal office BP but High home or ABPM Masked hypertension	High office BP and High home or ABPM True uncontrolled or resistant HTN	Normal office BP But High home or ABPM Masked uncontrolled hypertension or masked resistant HTN

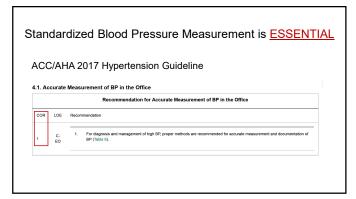
Hypertension Phenotypes more common in CKD than in the general population				
Untreated patients		Treated patients		
N	Normal office BP and ormal home or ABPM Sustained normotension	High office BP but Normal home or ABPM White coat hypertension	Normal office BP and Normal home or ABPM True BP control	High office BP but Normal home or ABPM White coat effect (white coat uncontrolled HTN)
i	High office BP and High home or ABPM Sustained hypertension	Normal office BP but High home or ABPM Masked hypertension	High office BP and High home or ABPM True uncontrolled or resistant HTN	Normal office BP But High home or ABPM Masked uncontrolled hypertension or masked resistant HTN

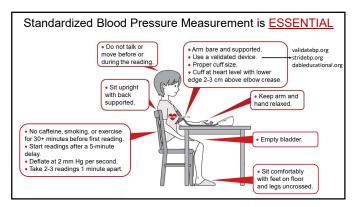


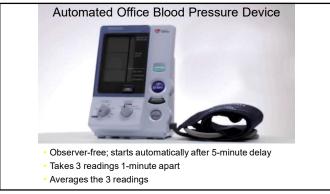
Prevalence of resistant hypertension is inversely related to GFR Prevalence of resistant hypertension per GFR A: Tanner RM et al. Clin J Am Soc Nephrol 2013;8:1583-90 B: Thomas G et al. Hypertension 2016;67:387-396. An J et al. CJASN 2022;17(Oct):1457-66 Kaiser Permanente + VA Health Admin.

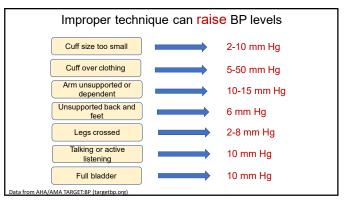












Adherence to proper technique is uncommon in primary care practice

26 primary care practices in Geneva, Switzerland Mean difference in BP between PCP and research assistant <u>after PCP training</u>: 23 mm Hg SBP and 14 mm Hg DBP

• Common errors

Back unsupported	50%
Arm unsupported	64%
Center of cuff not over brachial artery	52%
Single blood pressure reading	83%

Sebo P et al. J Hypertension 2014;509-517

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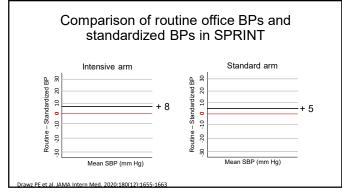
Why is standardized measurement essential?

• All clinical trials on which current guideline BP targets are based used standardized office BP measurements.

Clinical Trial	Method	Rest (minutes)	# of readings
SPRINT	AOBP	5	3
SPS3	AOBP	15	3
ADVANCE	AOBP	5	2
ACCORD	AOBP	5	3
ONTARGET	AOBP	3	2
AASK	Manual	5	3
MDDD	Manual	5	2

AOBP = Automated Office Blood Pressure measurements

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So, can subtracting 5-10 mm Hg from routine BP approximate standardized BP? Intensive arm Standard arm - Standardized BP -20 0 20 40 60 - Standardized BP -20 0 20 40 60 + 45 + 45 - 30 - 30 Routine – -60 -40 -4 Mean SBP (mm Hg) Mean SBP (mm Hg) In only 44% did the difference fall within 5-15 mm Hg In only 34% did the difference fall within 5-15 mm Hg

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The hazards of routine BP measurements

- Hazards of over-treatment of hypertension
 - Postural hypotension → debilitating symptoms
 - Recurrent falls and fractures
 - Stroke in patients with carotid obstructive disease
 - \bullet Acute kidney injury, esp. in those with renovascular disease
- Hazards of under-treatment of hypertension
 - Uncontrolled hypertension
 - Ischemic heart disease
 - · Heart failure
 - · Chronic kidney disease

Remember: CKD patients are at the highest risk for adverse CV outcomes.

...They stand to benefit the most from accurate BP measurements.

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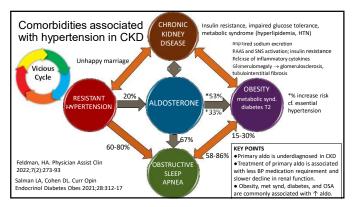
ButAre standardized BP measurements feasible in a primary care practice?

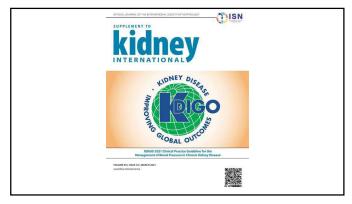


- Equipment
 AOBP devices can free up staff and provider time
 - Proper cuff sizes available (>40% of patients need a large cuff)
 - Upfront costs may pay off in the long-term
- Staff education

 - Train and re-train in proper BP technique
 Stress importance of accurate BP measurements
- Workflow
- Bring patients in 15 minutes before visit
- · Have patients fill out medical information ahead of visit
- Patient education

 - Wear clothing that allows arm to be exposed
 Don't smoke, exercise, drink caffeine 30 minutes before visit.
 - Empty bladder before entering exam room





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KDIGO Recommendation for Blood Pressure Target

Recommendation 3.1.1.
"We suggest that adults with CKD and high BP be treated with a target systolic blood pressure (SBP) of less than 120 mm Hg using standardized office BP measurement (2B)."

KDIGO Recommendation for Blood Pressure Target

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"We suggest that adults with CKD and high BP be treated with a target systolic blood pressure (SBP) of less than 120 mm Hg using standardized office BP measurement (2B)."

2 = weak recommendation

B = moderate quality of evidence

Based on a subset of participants in a single RCT (SPRINT)

Uncertain benefit in CKD patients excluded from SPRINT:

Diabetes, GFR <30 ml/min, SBP <130 mm Hg or >180 mm Hg,

very low DBP, age ≥85, very frail or institutionalized, proteinuria >1g/day

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KDIGO vs. ACC/AHA



ACC/AHA: "Adults with hypertension and CKD should be treated to a BP goal of less than 130/80 mm Hg (1B)."

The SBP target (<130 mm Hg) is higher than in SPRINT because:

- Entry criteria in RCTs limit extrapolation to a more general population.
- Standardized BP measurements in RCTs are lower than in clinical practice.

KDIGO: "We suggest that adults with CKD and high BP be treated with a target systolic blood pressure (SBP) of less than 120 mm Hg using standardized office BP measurement (2B)."

- There are no outcomes trials supporting a target of <130 mm Hg.
- Patients should **not be penalized** for suboptimal clinical practice.

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KDIGO Recommendation for Blood Pressure Target

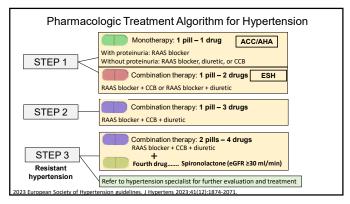
Recommendation 3.1.1:

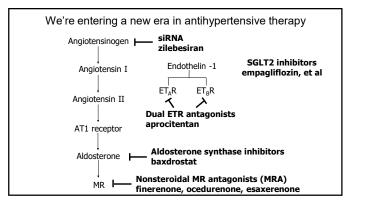
"We suggest that adults with CKD and high BP be treated with a target systolic blood pressure (SBP) of less than 120 mm Hg using standardized office BP measurement (2B)."

Practice Point 3.1.1:

"It is potentially hazardous to apply the recommended SBP target of less than 120 mm Hg to BP measurements obtained in a non-standardized manner."

	ACC/AHA	KDIGO
	2017	2021
Definition of hypertension	≥130/≥80	"High BP" is defined as a BP above target.
BP threshold for drug intervention	130/80 (with lifestyle modifications)	BP above target (with lifestyle modifications)
	<130/<80	SBP <120
	Deviates from SPRINT SBP	(no DBP target)
BP target	<120 to prevent hypotension if	Adheres strictly to SPRINT based on
	casual BP measurements are	obligatory use of standardized
	used	BP measurements
-	Strong recommendation to	Weaker recommendation: use HBPN
Out of office BP	confirm the diagnosis of	or ABPM to "complement
(HBPM or ABPM)	hypertension and for titration of	standardized office BP readings
	BP lowering medication	for the management of high BP"





Clinical Trials with New Antihypertensive Agents				
Reference	Drug, number and type of patients	Mechanism of action	Trial Phase and placebo-adjusted mean BP reduction (mm Hg)	Comments
Hypertens 2022 79:2685-95 J Hypertens 2023 41:295-302	Finerenone, 5669; T2D and CKD Finerenone, 239; T2D and CKD	Nonsteroidal MR antagonist	Phase 3 (office BPs) SBP 2-3; DBP 1 Phase 2b (24h ABPM) SBP 10; no DBP reported	Low rate of 个K ⁺ requiring D/Cing drug despite RAAS blockers. Cardiorenal benefits
NEJM 2023 389:228-238	Baxdrostat, 248; Resistant HTN (eGFR >45; av 85)	Blocks aldosterone synthesis	Phase 3 (office BPs) SBP 11; DBP 5 (with highest dose)	No inhibition of cortisol synthesis. Rare incidence of 个K+
Lancet 2022 400:1927-37	Aprocitentan, 730; Resistant HTN (some had ↑UACR and/or ↓eGFR)	Blocks action of endothelin, a potent vasoconstrictor	Phase 3 (office BPs + ABPM) SBP 4-5; DBP 4-5	Edema 9-18%; a few had HF hospitalization. Pts with CKD stage 3-4 had greater ↓ in SBP.
NEJM 2023 389:228-38	Zilebesiran, 107; hypertension but no CKD	Blocks hepatic production of angiotensinogen	Phase 1 (office BPs + ABPM) SBP 22; DBP 11 (with highest dose per ABPM)	Dosed s.q. Q 6 mos. No $\uparrow K^+$, \uparrow creatinine, or hypotension

Take-home Points

- Hypertension and chronic kidney disease share a pathogenetic bidirectional relationship that leads to cardiovascular morbidity and mortality.
- \bullet UACR is a harbinger of CV and CKD progression. Measure it in high-risk patients.
- Chronic kidney disease is associated with high-risk hypertension phenotypes, including masked, nocturnal, sustained, and resistant hypertension.
- Blood pressure is a vital sign. It must be measured accurately using a standardized protocol. To do otherwise is hazardous.
- Hypertension and chronic kidney disease are closely linked to other cardiovascular risk factors, including aldosterone, obstructive sleep apnea, and obesity-related metabolic disorders.
- The ACC/AHA and KDIGO guidelines both stress the importance of standardized blood pressure measurements but depart in the target blood pressure for chronic kidney disease patients: ACC/AHA <130/<80; KDIGO <120 systolic.
 ACC/AHA also places more emphasis on out of office BP's for Dx and Rx.

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