NephU™
Improving Awareness & Patient Outcomes

Hypertension & Kidney Health

Comparing Autosomal Dominant Polycystic Kidney Disease (ADPKD), Chronic Kidney Disease (CKD), & The General Population (GP)

Proposed Hypertension (HTN) Mechanisms

	ADPKD	CKD	GP
Proposed Mechanisms	⬆ Cyst growth → intrarenal vascular ischemia and renin angiotensin aldosterone system (RAAS) activation[1,2] • Endothelial dysfunction & diastolic dysfunction[2]	⬆ Sodium retention and extracellular volume expansion, peripheral vasoconstriction, upregulation of RAAS, endothelial dysfunction, and arterial stiffness[3]	Genetic and modifiable risk factors, such as diet, physical inactivity, alcohol consumption, overweight or obesity, excess sodium, low potassium intake, etc.[4,5]
	⬆ Diastolic dysfunction and left ventricular mass index (LVMI)[1,2,6]		
	⬆ Prevalence of nocturnal blood pressure (BP) non-dipping → ⬆organ damage risk[1]		
Clinical Presentation	• HTN mean onset at 30-34 years. 15 years earlier than GP[1,2] • Higher HTN prevalence in ADPKD patients compared to healthy individuals <45 years old in GP.[6] Men > women[1,2]	Prevalence ranges from 60–90% depending on the stage of CKD and its cause[3]	Prevalence increases significantly with increasing age and is higher in black patients than in white, Asian, and Hispanic Americans[4,5]
Complications	Cardiovascular morbidity (myocardial infarction, heart failure, aneurysms, stroke, etc.) and mortality, CKD progression, etc.[1-3]		

Recommended HTN Management

	ADPKD	CKD	GP
Lifestyle Modifications 1st-line	• **Sodium:** <2g/day or <5g sodium chloride/day[12], protein restriction to 0.8–1.0 g/kg ideal body weight[14] • **Dietary Approaches to Stop Hypertension (DASH Diet):** ⬆ fruits and vegetables, ⬇ saturated and unsaturated fats.[13] **CKD 4&5:** Hyperkalemia concern.[12] • **Fluids:** Moderate Alcohol (≤2 drinks for men, ≤1 for women)[3] ⬇ Caffeine Intake,[1,13] **Hydration goal for ADPKD:** ~3L/day.[1,11] • **Smoking Cessation**[1,3,12,13] • **Weight Loss:** waist-to-height ratio <0.5 to avoid obesity[13] • **Exercise:** 90-150 minutes of aerobic exercise weekly[3]		
Medications	**1st-line:** Angiotensin Converting Enzyme Inhibitors or Angiotensin 2 Receptor Blockers (ACE-I/ARB)[1,2,14] **2nd-line:** Beta blockers (mild RAAS effect)[1] **3rd-line:** Calcium channel blockers (CCB) with caution[1] **4th-line:** Diuretics with caution (+RAASi)[1]	**1st-line:** ACE-I/ARB for patients with high BP, CKD and severely or moderately increased albuminuria with or without diabetes[12] **Other drugs:** Based on comorbidities[3]	• Thiazide diuretics, ACE-I/ARB, CCB (choice based on comorbidities)[4,5] • For Stage II HTN (>140/90 mmHg), can consider starting with 2 agents from two different classes[4,5]
Goals	• **KDIGO*:** Systolic Blood Pressure (SBP) 95–110 mmHg may be more beneficial than 120–130 mmHg[12] • **Expert Opinion:** Mayo Class 1C-1E & 18-50 y.o.: <110/75 mmHg; others: <130/80 mmHg[14]	**KDIGO:** SBP <120 mmHg, if tolerated[12]	• **2017 Multisociety Guideline:** <130/80 mmHg for adults 18-65 y.o.[3,4,13] • **ISH*:** <65 y.o.: <130/80 mmHg, but >120/70 mmHg; >65 y.o.: <140/90 mmHg as tolerated[3,13]

HTN IN ADPKD

HTN is the first ADPKD complication in **30%** of patients[1]

HTN affects **20%** of ADPKD patients < 20 years old[1]

> 60% of ADPKD patients (all ages) have HTN prior to kidney function decline[2]

Earlier onset is linked to a *PKD1* mutation and a parent having ADPKD and HTN[1,2]

Hypertensive ADPKD patients with preserved kidney function have:

- ⬆ Greater total kidney volume (TKV)[2]
- ⬆ Higher proteinuria[2]
- ⬇ Decreased renal blood flow[2]

LANDMARK TRIALS

- **HALT-PKD Study A (2014)**[7] Intensive BP control (95-110 /60-75 mmHg) associated with slower TKV increase, kidney and cardiac function decline
- **HALT-PKD A Secondary Analysis (2018)**[8] Intensive BP control more effective than high dose RAAS blockade drugs at slowing TKV and eGFR decline
- **HALT-PKD Study B (2017)**[9] No significant difference in blood pressure & kidney function decline when treated with ACEi + placebo vs. ACEi and ARB drug
- **SPRINT Trial (2015)**[10] Trial stopped early when intensive treatment (SBP < 120) showed lower fatal and non-fatal major CV events and all-cause mortality but side effects higher in intensive treatment group
- **PREVENT-ADPKD (2021)**[11] Prescribed water intake vs. ad lib water intake did not cause significant improvement of height-adjusted TKV, kidney function decline, or copeptin levels

Abbreviations: Kidney Disease Improving Global Outcomes (KDIGO); 2020 International Society of Hypertension Global Hypertension Practice Guidelines (ISH); years old (y.o.)

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