

Proposed

Clinical

Mechanisms



Hypertension & Kidney Health

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



Proposed Hypertension (HTN) Mechanisms

ADPKD



CKD





HTN is the first ADPKD complication in 30% of patients1

HTN IN ADPKD

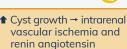
HTN affects 20% of ADPKD patients < 20 years old1

> **60%** of ADPKD patients (all ages) have HTN prior to kidney function decline²

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 proteinuria²
- Decreased renal blood $flow^2$



(RAAS) activation^{1,2} • Endothelial dysfunction & diastolic dysfunction²

aldosterone system

★ Sodium retention and extracellular volume expansion, peripheral vasoconstriction, upregulation of RAAS. endothelial dysfunction,

and arterial stiffness3

Genetic and modifiable risk factors, such as diet, physical inactivity, alcohol consumption, overweight or obesity, excess sodium, low potassium intake, etc.4,

♠ Diastolic dysfunction and left ventricular mass index (LVMI)^{1,2,6}

- ♠ Prevalence of nocturnal blood pressure (BP) non-dipping → **1** organ damage risk¹
- HTN mean onset at 30-34 years. 15 years earlier than GP1,2
- 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 cause³

Prevalence increases significantly with increasing age and is higher in black patients than in white, Asian, and Hispanic Americans^{4,5}

Complications

Lifestyle

1st-line

Modifications

Presentation

Cardiovascular morbidity (myocardial infarction, heart failure, aneurysms, stroke, etc.) and mortality, CKD progression, etc.1

Recommended HTN Management

ADPKD











• Sodium: <2g/day or <5g sodium chloride/day¹², protein restriction to 0.8–1.0 g/kg ideal body weight14 • Dietary Approaches to Stop Hypertension (DASH Diet): 1 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 obesity¹³
- Exercise: 90-150 minutes of aerobic exercise weekly³

Medications

Goals

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 caution1 4th-line: Diuretics with caution (+RAASi)1

KDIGO*:

Systolic Blood Pressure (SBP) 95-110 mmHq may be more beneficial than 120-130 mmHg¹²

Expert Opinion: Mayo Class 1C-1E & 18-50 y.o.: <110/75 mmHg; others: <130/80 mmHg¹⁴

1st-line: ACE-I/ARB for patients with high BP, CKD and severely or moderately increased albuminuria with or without diabetes12

Other drugs: Based on comorbidities3

KDIGO:

SBP <120 mmHg, if tolerated12

- 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 classes4,5
- 2017 Multisociety **Guideline:**
 - <130/80 mmHg for adults 18-65 y.o.^{3,4,13}

<65 y.o.: <130/80 mmHg, but >120/70 mmHg; >65 y.o.: <140/90 mmHq as tolerated 3,13

LANDMARK TRIALS

- HALT-PKD Study A (2014)⁷ Intensive BP control (95-110 /60-75 mmHq) 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

- Abbreviolatins: Rutiley Insease, Implicitly
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