Autosomal Dominant Polycystic Kidney Disease (ADPKD)

WHAT IS ADPKD?

A group of dominantly inherited disorders associated with kidney cysts and extra-renal manifestations caused by a pathogenic variant in a ADPKD gene.

Causal Genes

- *PKD1, PKD2* (account for >90% genetically resolved cases)
- *IFT140, ALG5, ALG9, GANAB, DNAJB11, NEK8*
- *ALG6, ALG8, PKHD1* (pathogenicity is uncertain)

Typical Phenotype

- Multiple, bilateral kidney cysts
- Progressive kidney enlargement
- Hypertension
- CKD G3
- Kidney failure in mid-to-late adulthood

HOW TO DIAGNOSE?

- Abdominal imaging by ultrasound
- ± Family history
- ± MRI or CT imaging
- ± Genetic testing
- Clinical phenotype (kidney pain, hematuria, hypertension, UTI, aneurysm, etc.)

WHEN IS GENETIC TESTING HELPFUL?

- Equivocal diagnosis based on kidney imaging
- Negative or unknown family history
- Atypical clinical presentation
  - Very early-onset cystic kidney disease
  - Syndromic features
- Discordant imaging and kidney function decline
- Variable disease severity in a family
- Young (<30 years old) living-related kidney donor workup
- Family planning
- Preimplantation diagnosis

*Genetic testing result may provide prognostic information and better risk stratify patients for disease-modifying therapy

PROGNOSTICATION TOOLS

- **Height-adulted total kidney volume (htTKV)** most accurately measured by MRI or CT scan predicts future decline in kidney function
- **Mayo Imaging Classification (MIC)**
  - Divides htTKV/age into 5 different classes to predict future decline in kidney function and the timing of kidney failure
  - Class 1 Typical ADPKD
    - 1A to 1E (from best to worst prognosis)
  - Class 2 Atypical ADPKD (predictive nature of MIC likely does not apply)
- **PROPKD score**
  - Use sex, hypertension or urologic event before age 35 years, pathogenetic variant

DELAY KIDNEY DISEASE PROGRESSION

Blood pressure control

- Use RASi (renin-angiotensin system inhibitor)
- Targets
  - Age 18–49 + CKD G1-G2: ≤110/75 mmHg (measured by HBPM, if tolerated)
  - Age ≥50 ± CKD G1–G5: SBP <120 mmHg (measured using standardized office BP measurement)

Water intake

2-3L daily (or more in hot climate conditions) in those with eGFR ≥30 ml/min per 1.73 m2 and without contraindications to excreting a solute load

Tolvaptan

Use in adults with ADPKD with eGFR ≥25 ml/min/1.73 m2 who are at risk for rapidly progressive disease (indicated by either MIC 1C to 1E or historical rate of eGFR decline ≥3 ml/min/1.73 m2 per year) and without contraindications

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COMMON RENAL COMPLICATIONS

**Only applicable for people with PKD1 or PKD2 if genetic information is available*

- Microscopic and macroscopic hematuria
- Hypertension
- Gout
- Kidney stones
- Cysts hemorrhage
- Cysts infection/urinary tract infections
- Kidney/Loin pain

EXTRA-RENAL MANIFESTATIONS

- Intracranial aneurysms or subarachnoid hemorrhage
- Mitral vale prolapse/regurgitation
- Pericardial effusion
- Abdominal wall hernia
- Dilated extrahepatic bile duct
- Bronchiectasis
- Pleural effusion
- Seminal vesicle cysts

ADDITIONAL CONSIDERATIONS

Intracranial Aneurysm

- **Patient education**
  - Educate all patients on the alarming symptoms of intracranial aneurysm (ICA), subarachnoid hemorrhage (SAH), and thunderclap headache and advised on immediate medical attention
  - Stop smoking
  - Optimize BP control
- **Who should be screened?**
  - Recommended in individuals with a personal or a positive family history of ICA, SAH, or unexplained sudden death who are eligible for treatment and with reasonable life expectancy
  - Discuss in patients with *de novo* ADPKD, uncertain family history, known personal or family history of extracerebral vascular phenotype, before major elective surgery, kidney/liver transplantation, or pregnancy planning, or in those not at high risk who prefer to be screened after understanding the limitations of screening
  - If screening is negative in high risk patients, timing of rescreening after a negative imaging should be individualized, possibly 5-10 years, based on risk factors, age and life expectancy.

Women of Childbearing Age

- **Hormonal therapy**
  - Counsel patients about risk/benefit of estrogen/progesterone therapy (i.e., exposure of which may increase the risk of PLD progression)
  - IUDs and gestagen OCPs may be preferred in women with PLD
- **Preconception counselling**
  - Potential teratogenic drugs should be discontinued (e.g., RASi, tolvaptan)
  - Explore and educate on risks of preeclampsia, pregnancy-induced hypertension, premature delivery
  - Genetic counselling at expert center
- **Pregnancy management**
  - Regular monitoring of BP, kidney function, proteinuria, UTI screening
  - Week 12-36: low dose aspirin is recommended
- **Post-delivery management**
  - Tolvaptan is contraindicated during breastfeeding
  - Some ACEi (enalapril/captopril) can be used with careful monitoring due to low penetration into human milk, if alternatives have been exhausted

References:

Kidney Disease: Improving Global Outcomes (KDIGO) ADPKD Work Group. "KDIGO 2025 Clinical Practice Guideline for the Evaluation, Management, and Treatment of Autosomal Dominant Polycystic Kidney Disease (ADPKD)." Kidney international vol. 107,2S (2025): S1-S239. doi:10.1016/j.kint.2024.07.009

For funding and support information, see: https://www.theisn.org/initiatives/rare-kidney-diseases-toolkit/#Support