

# Imaging Methodology:

## Ultrasound, CT, and MRI for imaging in ADPKD

ADPKD, autosomal dominant polycystic kidney disease; CT, computed tomography; MRI, magnetic resonance imaging.

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# Imaging Techniques for Measuring Kidney and Cyst Volumes in ADPKD

## Ultrasound

### Measurement accuracy:

- Can detect cysts >1 cm in diameter
- Large variations in kidney volume measurements due to inter-operator variability

### Advantages:

- Widely available
- Low cost
- Safety
- Well established diagnostic criteria

### Drawbacks:

- Lacks precision and accuracy for detecting short-term changes in kidney volume

## MRI

### Measurement accuracy:

- Can detect cysts  $\geq 2$ mm with smaller variations in kidney volume measurements

### Advantages:

- Can reliably measure TKV over short periods of time with minimal inter and intra-operator variability
- Allows quantitative assessment of disease severity (segmentation of cysts)
- Provides high-resolution and tissue-contrast 3D images

### Drawbacks:

- Cost and lack of availability
- Time needed for image acquisition

## CT

### Measurement accuracy:

- Can detect cysts  $\geq 2$ mm

### Advantages:

- Provides accurate and reliable measurements of TKV and cyst volume
- Correlates well with values obtained by ultrasound

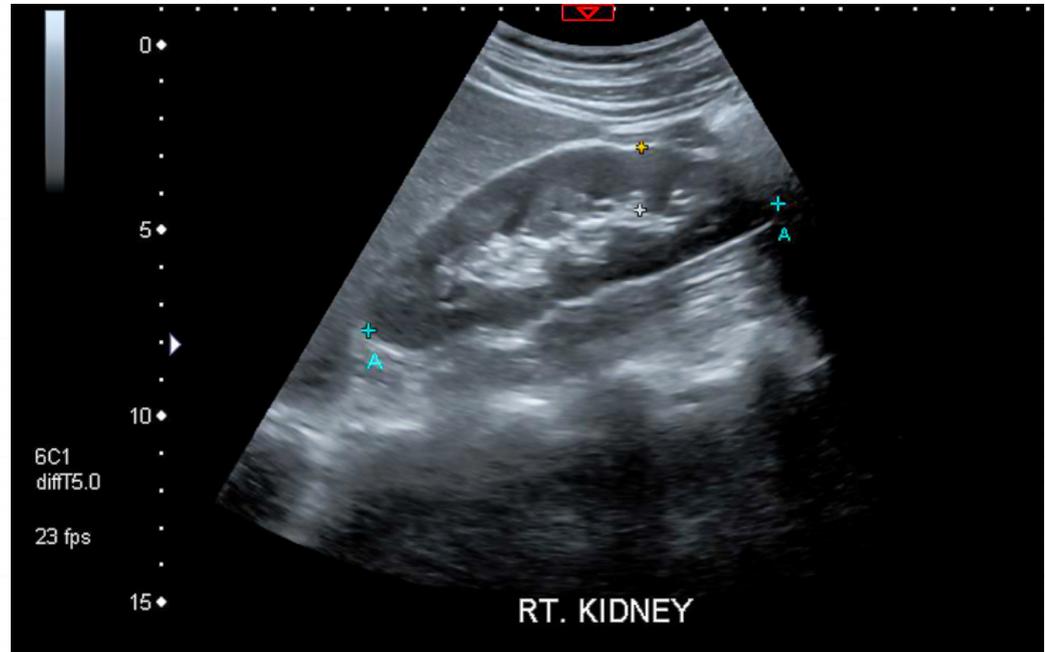
### Drawbacks:

- Potentially nephrotoxic contrast medium
- Exposure to ionizing radiation

Magistrini R et al. *Am J Nephrol.* 2018;48:67-78.

# Ultrasound is the Most Common Method Used for Diagnosis of ADPKD

- Sonographic features confirm diagnosis in the setting of positive family history<sup>1</sup>
- Commonly used due to low cost and safety<sup>2</sup>
- Visualization can be challenging in patients with abundant adipose tissue or bowel gas<sup>3</sup>
- Can be difficult and time-consuming to characterize small cysts<sup>3</sup>

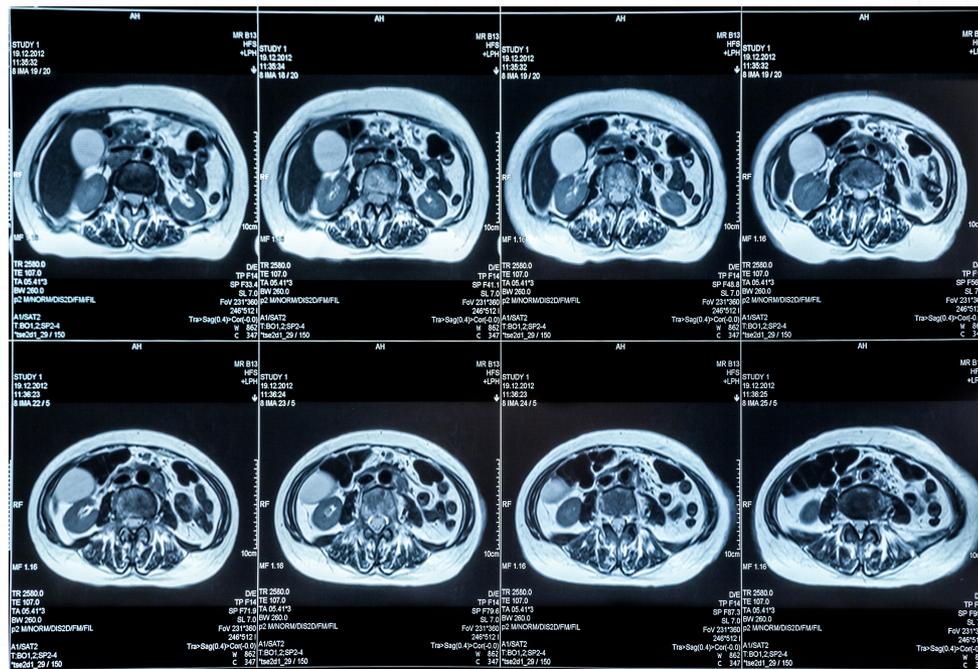


ADPKD, autosomal dominant polycystic kidney disease.

1. Barua M, Pei Y. *Semin Nephrol.* 2010; 30(4): 356–65.
2. Torres VE, Harris PC. *Kidney Int.* 2009; 76(2): 149–68.
3. Nascimento AB et al. *Radiology.* 2001; 21(3): 628–32.
4. Saedi D et al. *Cases J.* 2009; 2(66): 1–4.

# CT and MRI for ADPKD Diagnosis

- CT and MRI may be useful when ultrasound results are equivocal or indeterminate<sup>1</sup>
  - Both techniques can detect smaller cysts than ultrasound<sup>2,3</sup>
- Limitations
  - Predictive utility in ADPKD not validated<sup>1</sup>
  - Ultrasound criteria cannot be extrapolated<sup>1</sup>
  - Risks of CT include radiation exposure and allergy to contrast medium<sup>3</sup>



ADPKD, autosomal dominant polycystic kidney disease; CT, computed tomography; MRI, magnetic resonance imaging.

1. Pei Y, Watnick T. *Adv Chronic Kidney Dis*. 2010; 17(2): 140–52.
2. Nascimento AB et al. *Radiology*. 2001; 221: 628–32.
3. Pei Y. *Clin J Am Soc Nephrol*. 2006; 1(5): 1108–14.

# Pei Criteria for Ultrasound Diagnosis of ADPKD

Age	Number of Cysts	Cyst Location
15–29 years	$\geq 3$	Unilateral or bilateral renal cysts
30–39 years	$\geq 3$	Unilateral or bilateral renal cysts
40–59 years	$\geq 2$	Cysts in each kidney
$\geq 60$ years	$\geq 4$	Cysts in each kidney

- The Pei criteria are used for testing individuals who are at risk for ADPKD and in whom the gene type (*PKD1* or *PKD2*) is unknown

ADPKD, autosomal dominant polycystic kidney disease; *PKD1/2*, polycystic kidney disease gene 1/2.  
Pei Y et al. *J Am Soc Nephrol*. 2009; 20(1):205-212.

# Ultrasound has High Positive Predictive Value and Specificity for ADPKD

## Criteria for positive diagnosis\*

- **Ages 15–29**
  - **Diagnosis criteria:**  $\geq 3$  cysts, unilateral or bilateral
  - *Sensitivity by family genotype:* Unknown, 81.7; *PKD1*, 94.3; *PKD2*, 69.5
- **Ages 30–39**
  - **Diagnosis criteria:**  $\geq 3$  cysts, unilateral or bilateral
  - *Sensitivity by family genotype:* Unknown, 95.5; *PKD1*, 96.6; *PKD2*, 94.9
- **Ages 40–59**
  - **Diagnosis criteria:**  $\geq 2$  cysts in each kidney
  - *Sensitivity by family genotype:* Unknown, 90.0; *PKD1*, 92.6; *PKD2*, 88.8
- **Ages 60+**
  - **Diagnosis criteria:**  $\geq 4$  cysts in each kidney
  - *Sensitivity by family genotype:* 100 for all genotypes

## Criteria for exclusion diagnosis

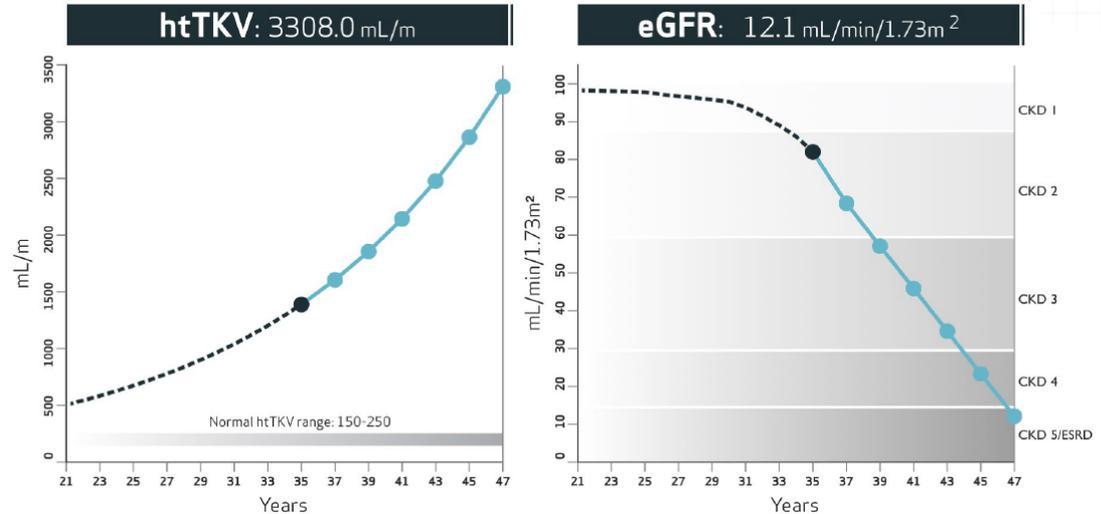
- **Ages 15–29**
  - **Diagnosis criteria:**  $\geq 1$  cyst
  - *NPV by family genotype:* Unknown, 90.8; *PKD1*, 99.1; *PKD2*, 83.5
  - *Specificity by family genotype:* Unknown, 97.1; *PKD1*, 97.6; *PKD2*, 96.6
- **Ages 30–39**
  - **Diagnosis criteria:**  $\geq 1$  cyst
  - *NPV by family genotype:* Unknown, 98.3; *PKD1*, 100; *PKD2*, 96.8
  - *Specificity by family genotype:* Unknown, 94.8; *PKD1*, 96.0; *PKD2*, 93.8
- **Ages 40–59**
  - **Diagnosis criteria:**  $\geq 1$  cyst
  - *NPV by family genotype:* 100 for all genotypes
  - *Specificity by family genotype:* Unknown, 93.9; *PKD1*, 93.9; *PKD2*, 93.7

\*PPV was 100 for each family genotype.

ADPKD, autosomal dominant polycystic kidney disease; NPV, negative predictive value; *PKD1/2*, polycystic kidney disease gene 1/2; PPV, positive predictive value. Pei Y, Watnick T. *Adv Chronic Kidney Dis.* 2010; 17(2): 140–52.

# Change in Kidney Volume in ADPKD Precedes Change in Renal Function

- The results of the CRISP study showed:
  - htTKV increased significantly from baseline each year, reaching a mean increase of 55% after 7.9 years of follow up<sup>1</sup>
  - GFR decline began in year 6 (-10.6%), and continued until year 8 (22.3%)<sup>1</sup>
- Among patients in the early stages of ADPKD, compensatory hyperfiltration adjusts for the loss of nephron function and ensures that GFR is maintained within normal levels until the fourth or fifth decade of life<sup>2</sup>

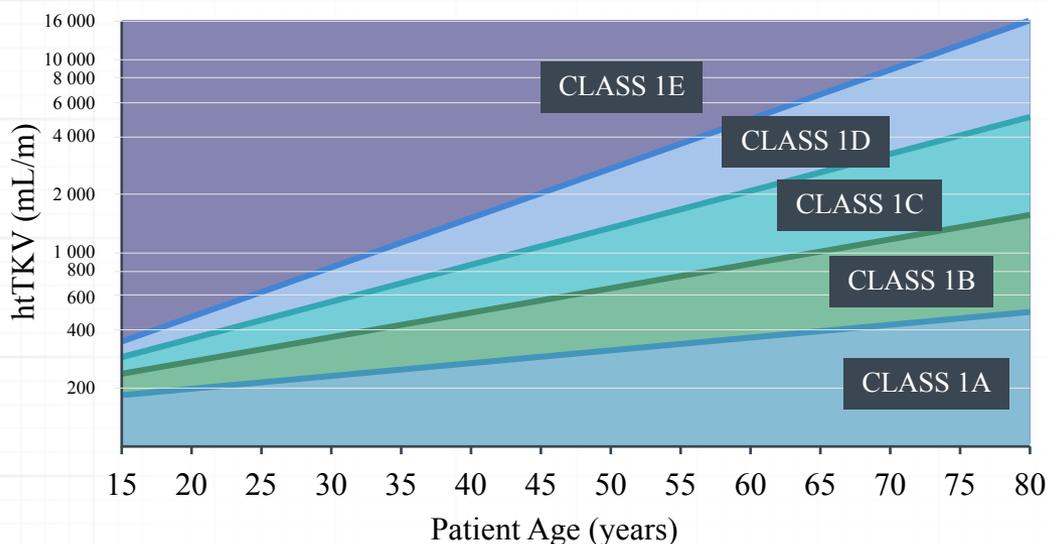


ADPKD, autosomal dominant polycystic kidney disease; CRISP, Consortium for Radiological Imaging Studies of Polycystic Kidney Disease; CKD, chronic kidney disease; ESRD, end-stage renal disease; eGFR, estimated GFR; GFR, glomerular filtration rate; htTKV, height-adjusted total kidney volume.

1. Chapman AB et al. *Clin J Am Soc Nephrol.* 2012; 7(3): 479–86.
2. Grantham JJ et al. *Clin J Am Soc Nephrol.* 2006; 1(1): 148–57.

# TKV-based Classification of ADPKD

Age and htTKV predicts decline in eGFR over time in patients with typical\* presentation of ADPKD



Class	Estimated kidney growth rate: yearly percentage increase	Risk for eGFR decline
1E	>6.0%	High risk
1D	4.5 – 6.0%	High risk
1C	3.0 – 4.5%	High risk
1B	1.5 - 3.0%	Intermediate risk
1A	<1.5%	Low risk

\*Typical presentation refers to patients with a bilateral and diffuse cyst distribution in both kidneys with mild to severe replacement of kidney tissue by cysts, with all cysts contributing similarly to TKV.

ADPKD, autosomal dominant polycystic kidney disease; eGFR, estimated glomerular filtration rate; htTKV, height-adjusted TKV; TKV, total kidney volume.

Irazabal MV et al. *J Am Soc Nephrol.* 2015; 26: 160-172.

# Ultrasound for the Measurement of Kidney Length

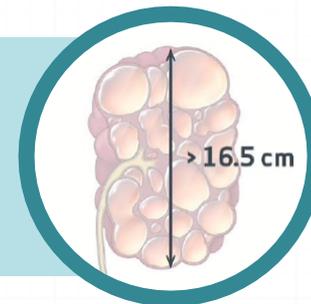
- MRI is the recommended imaging modality for the most accurate and reproducible measurement of KL, kidney cyst burden, and TKV<sup>1</sup>
- When MRI-calculated TKV is not feasible, US-measured KL has been proposed as a useful surrogate for identifying young ADPKD patients at risk of rapid progression<sup>1</sup>

**US-measured predictor of rapid progression<sup>†</sup>**

**KL > 16.5 cm**

**htTKV > 650 ml/m**

**in patients < 45 years old<sup>1,2</sup>**



## Limitations of US-KL in identifying rapid progression

- In data analysis, KL was not normalized for height, which is an important variable\*<sup>2</sup>
- Young patients with lengths < 16.5 cm may still have rapidly progressing disease<sup>3</sup>
- Atypical patients with slow progression may have lengths > 16.5 cm<sup>3</sup>
- US-measured KL is less accurate with larger kidneys<sup>1</sup>
- US measurements are operator-dependent and lack precision and accuracy for detecting short-term changes in kidney volume and increase the risk of misclassifying ADPKD progression<sup>1,3,4</sup>

\*Based on data analysis comparing US and MRI KL measurements from CRISP.<sup>1</sup> <sup>†</sup>When rapid progression is defined as CKD 3 development within 8 years.<sup>1,2</sup> ADPKD, autosomal dominant polycystic kidney disease; CKD, chronic kidney disease; CRISP, Consortium for Radiologic Imaging Studies of Polycystic Kidney Disease; htTKV, height-adjusted TKV; KL, kidney length; MRI, magnetic resonance imaging; TKV, total kidney volume; US, ultrasound.

1. Bhutani H et al. *Kidney Int.* 2015; 88:146-151.
2. Gansevoort RT et al. *Nephrol Dial Transplant.* 2016; 31:337-348.

3. Chebib FT et al. *J Am Soc Nephrol.* 2018; 29(10):2458-2470.
4. Magistroni R et al. *Am J Nephrol.* 2018; 48:67-78.

# Summary

- Total kidney volume predicts the risk of developing renal insufficiency in patients with ADPKD<sup>1,2</sup>
- MRI is the recommended imaging modality for the most accurate and reproducible measurement of KL, kidney cyst burden, and TKV<sup>3</sup>
- Ultrasound measures of kidney length and TKV are potential alternatives to MRI in the prediction of ADPKD progression<sup>3</sup>
  - Ultrasound is readily available and has fewer restrictions than MRI
- The optimal cutoffs for predicting progression to stage 3 chronic kidney disease within 8 years are<sup>3\*</sup>:

	Ultrasound	MRI
<b>htTKV</b>	650 ml	550 ml
<b>Kidney Length</b>	16.5 cm	16 cm

\*Based on data from CRISP.

ADPKD, autosomal dominant polycystic kidney disease; CRISP, Consortium for Radiologic Imaging Studies of Polycystic Kidney Disease; htTKV, height adjusted TKV; KL, kidney length; MRI, magnetic resonance imaging; TKV, total kidney volume.

1. Chapman AB et al. *Clin J Am Soc Nephrol*. 2012; 7(3): 479–86.
2. Irazabal MV et al. *J Am Soc Nephrol*. 2015; 26: 160-172.
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