All about imaging in polycystic kidney disease

Poster No.: C-1243
Congress: ECR 2015
Type: Educational Exhibit
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Keywords: Outcomes, Cysts, Congenital, Education, Computer Applications-Detection, diagnosis, Complications, Ultrasound, MR, CT, Kidney, Abdomen
DOI: 10.1594/ecr2015/C-1243

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Learning objectives

• To describe the indications, comparative use and limitations of various imaging modalities for the diagnosis and management of complications in polycystic kidney disease (PKD).

• To list and discuss the differential diagnosis of PKD.
Background

Definition:

Inherited cystic kidney diseases, including **autosomal dominant polycystic kidney disease** (ADPKD) and **autosomal recessive polycystic kidney disease** (ARPKD), are the most common monogenetic causes of end-stage renal disease (ESRD) in children and adults. While ARPKD is a rare and usually severe pediatric disease, the more common ADPKD typically shows a slowly progressive course leading to ESRD in adulthood (1).

Incidence:

ADPKD is the most common hereditary kidney disease, occurs in one of 400-1000 live births, showing no predilection for a particular sex or race. (2,3)

ARPKD have a prevalence of 1 in 20,000 live births, the disease may manifest at any time from birth to adulthood, with a mean age at presentation of 2.5 years (4).

Genetics

ARPKD is the most common ciliopathy occurring in infants, affects the kidney and the liver to varying degrees. The renal disease consists of nonobstructive, fusiform, dilated renal collecting ducts with progressive cystic degeneration, associated with congenital hepatic fibrosis (CHF) and ductal plate malformation, which leads to portal hypertension (5-7). The disease is caused by mutations in the polycystic kidney hepatic disease 1 (PKHD1) gene located on chromosome 6 that encodes the protein fibrocystin-polyductin localizing to the primary cilia of epithelial cells lining the renal tubules and intrahepatic bile ducts (8, 9-11).

ADPKD is caused by a mutation in the gene PKD1 mapped to chromosome 16 in 85% of patients and a mutation in PKD2 mapped to chromosome 4 in the remaining 15%. (60) PKD1 encodes the protein polycystin-1 and PKD2 encodes polycystin-2. Both interact to form a calcium2+-channel receptor and are localized to primary cilia in the epithelial cells lining the renal tubules. The proteins are important in the differentiation, maintenance, and repair of renal tubular cells and in determining the morphology of renal tubules (12,13).
Physiopathology

In ARPKD all renal cysts develop from focal epithelial proliferation along the course of the nephron and this occurs primarily in the collecting duct. Symmetric and circumferential epithelial proliferation results in tubular lengthening and fusiform dilatation of the collecting duct (14). The abnormal epithelium also manifests an unusual change in function and becomes secretory, whereas normal epithelium is essentially resorptive (15-17).

In contrast to ARPKD, the renal cysts in ADPKD may develop in any part of the nephron, so the cysts may involve the medulla and cortex. The cysts form as outpouchings of the nephron that become disconnected from the nephron early on and continue to grow, so that they are round rather than tubular (13).

Clinical features

ARPKD. More than one-half of patients with ARPKD - CHF have severe renal and are diagnosed prenatally (18). The symptoms include:

- large palpable flank masses
- small thorax
- respiratory distress and
- oliguria
- severe oligohydramnios that causes compressive effects on the fetus, constituting Potter sequence, with characteristic Potter facies and deformities of the extremities (clubfoot and congenital dislocation of the hips).

The survivals of neonatal period develop portal hypertension in childhood due to progressive periportal fibrosis, the clinically manifests are:

- hepatosplenomegaly
- hypersplenism with thrombocytopenia
- gastroesophageal variceal bleeding and
- ascites (19-21).

ADPKD is clinically silent in about half of affected people, and symptoms typically do not appear until after early to middle adulthood (age in the 30s to 60s) (3).

Renal manifestations:

- spontaneous or provoked abdominal or loin pain from cyst rupture;
- abdominal or flank masses;
• gross haematuria following abdominal trauma;
• hypertension: usually develops at the same time as renal failure;
• kidney infection and kidney stones;
• renal functional impairment to renal failure (22);

Extrarenal manifestations:

• cysts in other organs and tissue, liver is most affected (more than 85 percent of patients will have liver cysts by age 30.), over organs are pancreas, spleen, seminal vesicles, and arachnoid membrane;
• cardiovascular complications including intracranial aneurysms, aortic aneurysms, and aortic dissection (13);
• inguinal hernias and diverticular disease;

Radio-imaging methods and semiology:

Ultrasound (US)

The diagnosis of ARPKD can be suggested prenataally as early as 15 weeks gestation, imaging modalities of choice are US, especially high-spatial-resolution US. (23-25).

**US findings:** enlarged, smooth, hyperechogenic kidneys with lack of normal corticomedullary differentiation (26).

• Simple renal cysts will appear as multiple spherical, well-circumscribed, anechoic regions with good sound transmission.
• Cysts with haemorrhage or infection will demonstrate echogenic material within the cyst, without internal blood flow(6).

The high-spatial-resolution US (linear 7-9 MHz) distinguish: the collecting ducts, macroscopic cysts and hyperechoic foci, the last one matches to renal calcifications. The collecting ducts are described as dilated tubules with radial orientations to the kidney while the cysts as anechoic structures with imperceptible walls, with increased through -transmission, scattered randomly throughout the kidneys (25).

Renal ultrasound examination remains the preferred imaging modality for diagnosis of PKD and for family screening(1).

Computed tomography (CT)

**CT** is not the preferred examination for follow-up of ARPKD due to the risks of ionizing radiation and contrast agent-induced renal insufficiency.
NECT: bilateral renal enlargement, bosselated renal contour, and a variable but large number of cysts of varying size within both cortical and medullary regions. Simple, uncomplicated cysts are of homogeneous low density with attenuation values from -10 to +20 HU, show lack of contrast enhancement and have a distinct interface with surrounding renal parenchyma, presents smooth outer margins, and an imperceptibly thin cyst wall. Cysts which have internal complications present as multiple, sharply circumscribed, generally subcapsular lesions with attenuation values ranging from 60 to 90 HU (30). CECT. They do not enhance and are usually isodense or hypodense relative to remaining renal parenchyma on enhanced scans. The hyperdense appearance are the result of cyst hemorrhage followed by clot retraction and protein concentration. The cyst wall calcification develops as the blood clots liquefy and organize, cyst attenuation values gradually decrease (31).

**Magnetic resonance imaging (MRI)**

**MRI** described increased signal intensity of the renal parenchyma at T2-weighted imaging due to the large amount of urine in the dilated ducts (28). MR allows detailed depiction of the extent of kidney involvement without the risks of ionizing radiation and contrast agent-induced exacerbation of renal insufficiency (29).

Renal simple cysts appear morphologically the same as on CT, rounded well-defined structures with very thin regular walls, characteristically have a low signal on T1-weighted MR images and increase in intensity on T2-weighted sequences. MRI is very sensitive to characterize the hemorrhagic cysts in PKD- hyperintense on T1WI and T2WI in subacute stage. MRI allows estimate the renal and cyst volumes, which may be used as indicators of disease progression or treatment response (32).

The total kidney volume is calculated by using a stereologic method, after acquisition of coronal unenhanced T1, coronal T2 and coronal gadolinium-enhanced T1-weighted images with a section thickness of 3 mm, the area of the kidney measured on each section in the set of contiguous images is multiplied by the section thickness, and the products are then summed. (14) Overall increases in renal and cyst volumes are indicative of progression of the disease. MR imaging also allows accurate estimation of renal blood flow, thus a reduction in renal blood flow match with increase total kidney volume and is predictive of structural and functional disease progression (32).

**Diagnostic**

The *diagnosis of PKD* is based on a typical appearance on imaging, generally supported by a family history. The number of cysts required for a diagnosis is age-based and
increases in an age dependent manner given that simple acquired renal cysts occur with increasing frequency with age in the general population (1).

The diagnostic criteria after Pei-Ravine are: (1)

- the individuals of 15-39 years, with positive family history, present #3 (unilateral or bilateral)
- the individuals of 40-59 years, with positive family history, present #4 (at least 2 in each kidney)
- those aged 60 and above, with positive family history, present #8 (at least 4 in each kidney)
- the patients with no positive family history, at any age, that present #10 cysts in each kidney with renal enlargement ± hepatic cysts have a positive diagnosis.

Complications

- cyst hemorrhage
- cyst rupture
- cyst infection
- cyst calcification
- grafting of renal cell carcinoma
- kidney stones and
- urinary tract obstruction

Cyst hemorrhage. The factors leading to cyst hemorrhage are minor trauma, or occur randomly as part of the natural history of the disease (after heparinization during dialysis or secondary to arterial hypertension).

Cyst rupture. Often due to progressive cyst enlargement; if cysts are connected to the urinary collecting system the rupture make into the collecting system, and the ureters are intermittently obstructed by blood clots (16) or when located subcapsular the hemorrhage extension occurs into the perirenal space (13).

Kidney stones and urinary tract obstruction are the consequence or urinary stasis in the distorted collecting system (2).

Renal cell carcinoma. Renal carcinomas are rare, but are suggested on imaging by internal heterogeneity before or after intravenous contrast medium injection, contrast enhancement and irregular interfaces with renal parenchyma (22).

Differential diagnosis (34,35)

- ARPKD vs ADPKD
- Medullary cystic disease
- Acquired renal cystic disease
- von Hippel Lindau disease
- Tuberous sclerosis complex
• Multicystic dysplastic Kidney
• Simple renal cysts

**Autosomal dominant polycystic kidney disease**: bilateral enlarged kidneys with multiple expansile cysts.

**Autosomal recessive polycystic kidney disease**: kidneys are smoothly enlarged because of the numerous dilated collecting ducts. The degree of enlargement is directly proportional to the number of dilated ducts.

**Medullary cystic kidney disease**: multiple cysts at the corticomedullary junction and in the medulla.

**Acquired cystic kidney disease**: bilateral small kidneys with multiple cysts, increased risk of intracystic hemorrhage, and development of renal cell carcinomas.

**Von Hippel Lindau disease**: multiple, variably sized cysts in both kidneys; multiple interspersed cystic and solid renal cell carcinomas.

**Tuberous sclerosis complex**: multiple, bilateral renal cysts intermixed with multiple angiomyolipomas.

**Medullary sponge kidney**: medullary nephrocalcinosis and cysts, paint brushlike appearance, multiple renal calculi.

**Multicystic dysplastic kidney**: nonreniform, nonfunctional kidney with multiple peripheral cysts and central solid components.

**Localized renal cystic disease**: conglomerate mass of multiple simple cysts of various sizes, separated by enhancing or atrophic renal tissue and without a definite capsule.
Findings and procedure details

We reviewed imaging characteristics of polycystic kidney disease, the complications and differential diagnosis.

IMAGING TECHNIQUES

Ultrasound - we have used a convex probe (3.5 MHz) for the evaluation of deeper structures.

CT. Nonenhanced CT (NECT) evaluation (mono-/ and multislice) of the abdomen.

Multiphase contrast enhanced CT (CECT) in patients with normal renal function (1-1,5 ml/Kg of body; injected rate of 2,5-3ml/sec) using a cortico-medullary phase (35 sec), nephrographic phase (80 sec) and excretory phase (variable timing).

MRI

MR system with 1,5 T intensity field; body phased array coils (Torsopa)

- T2 FSE FS, T1 FSPGR FS wi pre-/ postcontrast injection
- MR-uography: ssFSE short TE /long TE
- Multiphase 3D T1 FSPGR Fat Sat +Gd (0,1 mmol/kg of body)-
- MR-uography after Gd injection and Furosemid iv inj.

IMAGING SIGNS

Ultrasound findings

US imaging in ARPKD reveals massively enlarged, smooth, hyperechogenic kidneys with lack of normal corticomedullary differentiation (Fig. 1 on page 12).

In ADPKD, sonogram shows simple cyst that appear as multiple anechoic lesion, with posterior acoustic enhancement. They vary in size, most of which have a diameter of 3cm or more, and are scattered throughout the cortex, including in medullar and subcapsular locations. In advanced stages of disease the size and number of cysts increase and the reniform shape is replaced with irregular outline (Fig. 2 on page 12).

CT findings
CT scan demonstrates multiple fluid rounded structures with very thin and regular wall, often imperceptible, without enhancement in child and adult. (Fig. 3 on page 13 and Fig. 4 on page 13). Cysts which have had internal complications, may be hyperattenuating, with internal non-enhancing septations and/or calcifications.

**MRI findings:**

On MRI simple cysts appear hypointense on T1 weighted images and hyperintense on T2 weighted images. (Fig. 5 on page 14). The cysts with modified content (proteic/hemorrhagic) appear hyperintense on T1 weighted sequences and hiper-hypointense in T2WI (Fig. 6 on page 15).

**Complications.** The most frequently complications were:

- cyst hemorrhage
- cyst rupture
- cysts wall calcification
- cyst infection
- renal cell carcinoma

**Intracystic hemorrhage** is shown as a high-attenuation mass (60 to 90 HU) on unenhanced CT scan. (Fig. 7 on page 16). On MRI the aspect of the hemorrhagic cyst depends on the stage of the hemorrhage (acute/subacute/chronic). Layering (blood fluid level) may be present that demonstrate recent intracystic bleeding (Fig. 8 on page 17).

**Hemorrhagic cyst rupture** appears on CT and MRI as a large perinephric hematic collection (Fig. 9 on page 18 and Fig. 10 on page 19).

**Cyst infection** presents on CT a thickened wall, that enhance, with or without modified content (Fig. 11 on page 20). On MRI, infected cysts appears with an intermediate signal intensity on T1 weighted and T2 weighted images.

**Cyst wall calcification** is better seen on CT. They appears as arcuate, curvilinear or pulverulent hyperdensity. (Fig. 7 on page 16). The inability to depict calcification is a distinct limitation of MRI, where calcification have no signal.

**Kidney stones.** Urinary stasis in the distorted collecting system plays a role in the pathogenesis of stone formation. US is generally the first modality of imaging for stones detection, but is not always simple because of renal anatomy deformity and presence of parenchymal and cyst wall calcifications. The modality of choice is unenhanced CT scan that demonstrate hyperdense lesion and can evaluate their exactly size and location (Fig. 12 on page 21).

**Renal cell carcinoma** are a rare entities, but can appears and yield to a diagnostic differential with a complicated cyst (Fig. 13 on page 21). However, there are distinctive CT criteria for differentiating these cysts from renal lesions requiring surgery:
solid renal tumors may appear denser than unenhanced normal parenchyma on CT, but they are generally less dense relative to kidney than the hyperdense cysts, are characterized by internal heterogeneity before and/or after intravenous contrast injection, enhancement on postcontrast scans and irregular interfaces with renal parenchyma.

**DIFFERENTIAL DIAGNOSIS.** Differential diagnosis must be done with:

- phakomatoses: von Hippel - Lindau and tuberous sclerosis complex
- parapelvic cyst
- bilateral hydronephrosis
- multiple simple kidney cysts
- acquired cystic kidney disease
- medullary sponge kidney

**Von Hippel - Lindau syndrome:** typical appearance are variably sized cysts in both kidneys, and interspersed cystic and solid renal cell carcinomas. (Fig. 14 on page 22).

**Tuberous sclerosis (TS):** renal lesions in TS are characterized by bilateral cysts intermixed with multiple angiomyolipomas (Fig. 15 on page 23).

**Bilateral parapelvic cysts:** are simple renal cysts located into the renal sinus. CECT in excretory phase and MR urography with Gd are crucial for the diagnostic (Fig. 16 on page 24).

**Bilateral hydronephrosis:** importance of the CT urography and MR-urography acquisitions (Fig. 17 on page 25).

**Multiple simple kidney cysts:** characterized by the development of simple, large fluid-filled cysts in the kidneys in individuals who have no history of hereditary cystic disease and negative genetic tests. Between the cysts, there is normal renal parenchyma (Fig. 18 on page 26).

**Acquired cystic kidney disease:** the entity is characterized by the development of numerous fluid-filled cysts in small kidneys (Fig. 19 on page 27).

**Medullary sponge kidney:** medullary nephrocalcinosis and cysts, paintbrushlike appearance, multiple renal calculi (Fig. 20 on page 28).
Fig. 1: ARPKD. Kidney ultrasound evaluation in a 8-year-old girl, shows massively enlarged right and left kidney that measures 15.4 cm, respectively 15.2 cm in length (a,c). The kidney is echogenic with loss of the normal corticomedullary differentiation and presence of hypoechoic cysts (arrow) (b,d). Foci of intense echogenicity (arrow head) may be due to the acoustic interfaces at the wall of tiny cysts or to focal renal calcification (b).

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**Fig. 2:** ADPKD. Ultrasound of the kidney in a 60-year-old woman with polycystic kidney disease shows multiple and conglomerate cysts of varying size and shape (a,b).

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**Fig. 3:** ARPKD. NECT (a) and CECT (b) in a 11-year-old boy shows massive enlargement of both kidneys which contains multiple and conglomerate cysts.

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**Fig. 4:** ADPKD. NECT (a) and CECT (b, c, d) of the abdomen in a 59-year-old man shows numerous cysts of different sizes involving the both kidneys and the liver. with complete replacement of renal parenchyma. Note also in the coronal plane reconstruction (d) a right renal graft (arrow head).

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Fig. 5: ADPKD. MRI sequences T1 FS (a), T1 w + GD (b), ssFSE short TE(c) and ssFSE long TE(d) in a 23-year-old woman depicts multiple bilateral simple cysts involving the corticomedullary renal parenchyma.

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Fig. 6: ADPKD. MRI evaluation by T1 FSPGR (a), T2 FS (b), T1 FS + Gd (c), ssFSE Short TE (d), ssFSE Long TE (e) in a 49-year-old man shows enlargement of both kidneys with multiple expansive renal cysts (arrow), most of them with fluid content and some with modified content (proteic and hemorrhagic) (arrow head).

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**Fig. 7:** Hemorrhagic cysts and pericystic calcifications in ADPKD. NECT (a) and CECT (b, c) scan in a 73-year-old woman displays high-density cysts in the right kidney (arrow). Note multiples nodular, linear and arcuate calcifications between the cysts (arrow head) (b).

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**Fig. 8:** ADPKD with multiple simple and modified cysts. MRI evaluation using T1 FSPGR (a), T2 FS (b), TE short (c), TE long (d) in a 39-year-old man depicts fluid level on the T1 FSPGR FS image zoomed (arrow).

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Fig. 9: ADPKD with ruptured left hemorrhagic cyst with subcapsular hematoma: ssFSE short TE (a), T1 FSPGR FS before (b) et after Gd iv inj (c); note also the modified content of others renal cysts which presents proteic and hemorrhagic content.

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**Fig. 10:** ADPKD with bilateral hemorrhagic cysts and left subcapsular hematoma- NECT (a,b) demonstrates multiple bilateral high-density cysts (arrow head); note also a large left subcapsular hematoma (arrow).

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**Fig. 11:** ADPKD with right cyst infection. CECT in a 40-year-old-woman with inflammatory signs show right renal cystic lesion with thickened, irregular walls (a) and thickening of the perirenal fascia (b). A control enhanced CT after antibiotic therapy demonstrate the disappearance of the cyst with persistence of a small band densification (c).
Fig. 12: Kidney stone in the ADPKD. NECT (a) and CECT (b) in a 55-year-old woman shows kidney stone in a middle calyx.

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**Fig. 13:** Right Grawitz tumor on ADPKD: NECT (a) and CECT (b, c). The cortico-medullary and nephrographic phase shows a heterogeneous right renal mass with cystic and tissular component (arrow).

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Fig. 14: Bilateral renal cystic lesions in von Hippel Lindau disease: CECT (a,b), MRI in T1 FSPGR FS+Gd (c,d)-note also the pancreatic cysts and the right renal cell carcinoma (T)

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**Fig. 15:** Renal cystic lesions in tuberous sclerosis: utility of ssFSE long TE and ssFSE short TE in the characterization of renal masses: multiple bilateral renal cysts (white arrow) and large right angiomiolipma (black arrow)

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Fig. 16: Bilateral large parapelvic cysts: NECT (a), CECT -nephrographic phase (b), excretory phase (c)- importance of the excretory phase for the diagnosis and the differential diagnosis with bilateral hydrenephrosis

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Fig. 17: Bilateral destructive ureterohydronephrosis- MR urography using ssFSE short TE (a) and long TE (b,c); note also the important dilatation of the urinary bladder

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**Fig. 18:** Simple kidney cysts. T1 FSPGR + Gd shows a few large cysts in both kidney with preservation of renal parenchyma between the cysts.

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**Fig. 19:** Chronic renal insufficiency. T1 FSPGR FS (a), ssFSE short TE (b) and long TE (c) demonstrate small kidney with renal sinus lipomatosis (left kidney) and numerous small bilateral fluid-filled cysts.

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**Fig. 20:** Medullary sponge kidney: medullary nephrocalcinosis and cysts, paintbrushlike appearance, multiple renal calcifications- NECT (a), T1WI Fat Sat+Gd.

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Conclusion

• The presence of multiple bilateral renal cysts is required for a diagnosis of PKD.
• US, CT and MRI are used to evaluate PKD.
• MRI demonstrates greater contrast resolution and increased sensitivity for detecting renal cysts less than one centimeter in diameter.
• However, US remain the initial modality for the diagnosis and the follow-up.
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