Diagnostic Imaging of Autosomal Dominant Polycystic Kidney Disease

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Summary

Autosomal dominant polycystic kidney disease (ADPKD) is one of the most common genetic disorders caused by a single gene mutation. The disease usually manifests itself at the age of 30–40 years and is characterized by formation of renal cysts along with the enlargement of kidneys and deterioration of their function, eventually leading to renal insufficiency.

Imaging studies (sonography, computed tomography, magnetic resonance imaging) play an important role in the diagnostics of the disease, the monitoring of its progression, and the detection of complications. Imaging is also helpful in detecting extrarenal manifestations of ADPKD, most significant of which include intracranial aneurysms and cystic liver diseases.

MeSH Keywords: Intracranial Aneurysm • Magnetic Resonance Imaging • Polycystic Kidney, Autosomal Dominant • Tomography, Spiral Computed • Ultrasonography

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Background

Autosomal dominant polycystic kidney disease (ADPKD) is one of the most common genetic disorders caused by single gene mutations and occurs in 1 in every 1000 individuals in the overall population, based on the number of clinical diagnoses. Including the cases diagnosed during autopsies, the mean estimated incidence is about 1 in 400 individuals. ADPKD is considered to be one of the main causes of renal insufficiency [1].

The disorder is passed down in autosomal dominant pattern with varied expression, albeit nearly always with 100% penetration of mutated genes PKD1 or PKD2. PKD1 gene was localized on the long arm of chromosome 16 (16p13.3-p13.12) as a gene encoding for polycystin-1 protein. PKD2 gene is located on the long arm of chromosome 4 (4q21-q23) and encodes for polycystin-2 protein. Both these transmembrane proteins are present within the primary cilia of renal tubular epithelial cells. Polycystin-1 is a ciliary mechanoreceptor while polycystin-2 is its coupled calcium channel. Abnormal structure and function of the cilia leads to disturbed function of the calcium channels, increased intracellular calcium, disturbed homeostasis, deregulated proliferation of tubular cells, dilation of tubules and development of renal cysts. Renal cysts in the course of ADPKD originate from about 1–2% of nephrons and may develop in any of the kidney segments [1]. As the disease progresses and cysts are enlarged, the remaining part of the kidney deteriorates gradually.

Mutation of PKD1 gene occurs in 85% of patients while mutation of PKD2 gene occurs in 15% of patients. In Polish population, mutation of PKD1 was observed in 95% of patients. Usually passed down in a dominant pattern, the disease occurs spontaneously without any family history in 5–10% of cases [2]. The risk of the disease being passed down to the offspring is 50%.

Clinical manifestations of the disease caused by the mutation of either of the genes is similar. However, PKD1 mutation is responsible for an earlier onset and more severe course of the disease. On average, end-stage renal disease developing from type 1 ADPKD develops 10 years earlier...
than in the case of type 2 ADPKD. Among the PKD1 mutation variants, individuals with mutation within the 5L region are affected in a more severe manner than patients with mutation within the 3L (18.9% vs. 39.7% of individuals with normal renal function at the age of 60). Intracranial aneurysms are also more common in the former group [3–5].

The disease is manifested at the age of about 30–40, and therefore is referred to in Polish as polycystic renal degeneration in adults (previously adult-type cystic kidney disease). It is associated with the development of numerous cysts progressing in an exponential manner [6,7]. Already in the initial period, renal blood flow becomes disturbed [8]. One of the first symptoms consists in poor urinary concentration; renal insufficiency develops at a later period [9].

Not only the kidneys are affected in the pathological course of ADPKD. Extrarenal manifestations include formation of cysts within other organs, most commonly liver, pancreas, and spleen. Seminal vesicle cysts and arachnoid cysts are also more common than in the general population.

Usually, ADPKD patients suffer from acute or chronic pains (mostly caused by infection or intracystic bleeding), hematuria, urinary tract infections, nephrolithiasis and arterial hypertension (occurring in all patients at later disease stages).

In some cases, the large, growing cysts are the direct cause of the pain.

Also observed are mitral valve prolapse, intracranial artery aneurysms or dolichoectasias, aortic aneurysms, abdominal (particularly inguinal) hernias, and diverticulitis. Due to the population of the study groups being too low and the disease being relatively rare, incidental concomitance of ADPKD with some of these pathologies (e.g. diverticulitis) is unlikely [10].

The clinical course and prognosis in ADPKD are affected not only by early detection, but also by the assessment of the kidney cyst enlargement process. The latter parameter determines the occurrence of arterial hypertension and decrease in glomerular filtration leading to secondary renal failure. Most important among the extrarenal disorders that accompany ADPKD are hepatic cysts and intracranial aneurysms. Other pathologies usually have no impact on the natural history of ADPKD.

**Diagnosis**

In ADPKD, the most sensitive diagnostic method consists in genetic testing. Currently, genetic testing is used only in research studies and in special clinical situations (e.g. as part of final diagnosis in a potential living kidney donor) [11–13]. This is due to the high cost and labor consumption of genetic tests compared with the relative ease of clinical diagnosis as well as to suboptimal sensitivity caused by a high number or possible mutation variants.

Therefore, basic components of diagnosis include the family history and diagnostic imaging. Diagnostic imaging examinations should be the standard of care in individuals at 50% risk of the disease, i.e. in the offspring and the siblings of affected individuals. The diagnosis of ADPKD usually consists in visualization of multiple cysts in an abdominal ultrasound scan (Figure 1). The methodology of the US scan is not different from that in the standard abdominal ultrasound scan, with no necessity for the scan to be performed in fasting condition. USG is characterized by high (nearly 90%) sensitivity of renal cyst detection, low cost, wide availability, high repeatability and lack of adverse biological consequences of the scan. All the above factors determine the widespread use of ultrasonography in the ADPKD diagnosis and progression monitoring.

Ultrasound-based diagnosis of type 1 ADPKD is based on Ravine’s criteria (Table 1). Their sensitivity approaches 100% both in patients above the age of 30 as well as in younger patients. The applicability of Ravine’s criteria in patients with PKD2 mutation is lower, particularly in the group below the age of 30 (in this case, the diagnostic sensitivity is about 67%) [14]. This is also true in patients with no family history of the disease, and therefore, the more accurate criteria developed by Demetriou et al. (Table 2) are recommended in suspected cases of type 2 ADPKD [15].

Pei et al. proposed a collective classification for ultrasonographic identification of both types of the disease to achieve the diagnostic sensitivity of as much as 93% in patients with positive family history of the disease (Table 3) [16]. According to these authors, detection of 2 or fewer cysts in individuals above 40 rules out the ADPKD. In addition, hepatic cysts were detected in 85% of ADPKD patients above the age of 30, possibly providing an important clue for the diagnosis of ADPKD in patients with negative family history.

![Renal US scan. Multiple cysts.](image)

**Table 1. Ultrasound-based Ravine’s criteria for type 1 ADPKD diagnosis.**

| Age (years) | Number of cysts |
|------------|----------------|
|            | Positive family history | Negative family history |
| <30        | At least 2 in one or both kidneys | At least 5 |
| 30–59      | At least 2 in each kidney | At least 5 |
| >60        | At least 3 in each kidney | At least 8 |

[1] © Pol J Radiol, 2016; 81: 441-453
history of the disease. Currently, Pei’s criteria of 2009 are used in patients with positive family history.

Ultrasonographic detection or exclusion of the disease in patients below the age of 14 is unreliable. In children below the age of 5, as much as 38% of ADPKD diagnoses were false negative while as much as 25% were false positive [17]; therefore, individuals with positive family history of ADPKD are recommended to undergo ultrasound scans only after reaching 20–30 years of age, when the relatively reliable diagnosis allows for appropriate prevention or effective treatment of potential complications.

In addition, precise determination of renal morphology and size is required along with the ultrasound detection and evaluation of cysts.

In ultrasonographic scans, renal cysts have characteristic features including circular or oval shape, smooth and thin walls, lack of calcifications, compartments, or thickenings, echo-free internal structure (no reflections of ultrasound waves) and posterior acoustic enhancement proportional to the size of the cyst. These features facilitate diagnosis of simple cysts [18].

The applicability of contrast-enhanced ultrasonography (CEUS) in ADPKD is not significant. Despite the fact that CEUS is better than conventional US and SC in visualization of cystic walls and compartments as well as of the presence of solid elements, diagnostic limitation in ADPKD patients consists in the kidneys being enlarged as well as in the high number of lesions morphologically different from simple cysts. However, in certain clinical cases, CEUS may provide a valuable supplement to US-based diagnostics.

Besides ultrasonic scans, diagnostic imaging techniques used in ADPKD patients include computed tomography (CT) and magnetic resonance imaging (MRI).

Renal CT scans are performed in supine position with hands raised above the body. Patients should be appropriately hydrated. The scans are acquired at inhale breath-hold and the scanning range is determined by the size of the kidneys; in end-stage disease, examination includes not only the upper part of the abdomen (down to the aortic bifurcation), but pelvis minor as well. Acquisition technique depends on the scanner type.

Scans dedicated to renal evaluation (particularly in ADPKD patients) should include in-phase images without contrast enhancement. These are acquired with the aim to detect small deposits and calcifications, bleedings, adipose tissue as well as to determine the baseline level for the contrast enhancement measurements. After intravenous administration of contrast agent, mono- or multiphase scans are acquired depending on the clinical problem. Scans should include the nephrographic phase, most useful in the assessment of focal lesions. In addition, corticomedullary phase (arterial phase for the assessment of bleeding and small, vascularized tumors) and excretory phase (for the assessment of pyelocalyceal systems) may be included. In patients with urinary stasis, significantly delayed phase scans may be required (>30 min after contrast administration).

Conventional renal MRI protocol includes T2-weighted images, chemical shift imaging (CSI, in-phase/anti-phase) sequences, and fat-saturated T1-weighted images before and after intravenous injection of paramagnetic contrast agent. Inclusion of dynamic contrast-enhanced MRI scans and DWI scans provides a multiparametric (MP) protocol of MRI examination that becomes the gold standard in renal MRI assessments. Inclusion of magnetic resonance urography (MRU) is also useful for the assessment of the pyelocalyceal systems [19]. MRU examination may be performed in dual manner: the first method consists in acquisition of hydrographic sequence visualizing static fluids based on heavily T2-weighted images. Several repetitions of this sequence (cine-MR urography) may be performed for better visualization of the pyelocalyceal systems and ureters. The other method consists in acquiring MRU scans after intravenous contrast administration; excretory function of kidneys must be conserved for this examination to be feasible. Administration of diuretics may be helpful, particularly in patients without pyelocalyceal system dilation [20]. Both urographic techniques are subject to significant limitations, particularly in patients with advanced-stage disease. In the hydrographic method, a large number of well-developed cysts obscures the contours of the pyelocalyceal system, whereas patients with advanced stage renal insufficiency have contraindications for parenteral administration of gadolinium contrast agents.

Blood oxygen level-dependent magnetic resonance imaging (BOLD-MRI), employing deoxyhemoglobin as an endogenous marker of tissue oxygen saturation, is a novel technique used in the assessment of certain renal pathologies. Interpretation of the results is difficult as the acquired BOLD-MRI signals depend e.g. on patient hydration, circulating blood volume, age, sex, factors affecting the oxygen dissociation curve (body temperature, hemocrit, blood pH) [21]. Results of pilot studies that examined the BOLD effects in chronic nephropathies, diabetic

| Age (years) | Number of cysts |
|------------|-----------------|
| 15–19      | One in each kidney or 2 unilaterally |
| 20–29      | >3 in total, at least 1 in each kidney |
| 30–59      | At least 2 in each kidney |
| >60        | At least 4 in each kidney |

Table 2. Ultrasound-based Demetriou criteria for type 2 ADPKD diagnosis in patients with a positive family history.

| Age (years) | Number of cysts |
|------------|-----------------|
| 15–39      | Total >3, uni- or bilateral |
| 40–59      | Total >4, at least 2 within each kidney |
| >60        | Total >8, at least 4 within each kidney |

Table 3. Pei’s criteria for ultrasonographic diagnosis of ADPKD in patients with positive family history.
nephropathy, ischemic nephropathy, acute renal injury (acute ischemia, contrast-induced nephropathy) and congestive nephropathy.

Both CT and MRI are characterized by high sensitivity of cyst detection, particularly with respect to cysts smaller than 1 cm in diameter. This is particularly true in case of detection of cyst-like lesions in T2-weighted MR images. At the same time, MRI is highly specific in diagnosing ADPKD (both the sensitivity and specificity of MRI scans in the diagnostics of ADPKD are 100%) [22]. Both methods are particularly useful in cases of negative family history when ADPKD should be diagnosed on identification of enlarged kidneys with multiple bilateral cysts, concurrent hepatic cysts and absence of symptoms of any other cystic kidney disease.

CT and MRI symptomatology of cystic lesions is quite typical.

In CT, cysts are thin-walled fluid-filled spaces with radiation attenuation coefficient typical to that of water (0–10 H.U.), not enhanced following intravenous contrast administration. The wall of a simple cyst should be free of thickenings (either diffuse or nodular), calcifications, internal compartments and solid elements enhanced following intravenous contract administration.

In MRI scans, simple cysts generate signals that are typical for water T2-weighted images with low signal appearance in T1-weighted images; cysts are not enhanced after contrast administration (increased signal intensity in T1-weighted images may be observed in the delayed phase after one hour due to the diffusion of the contrast agent through the cystic wall rather than from typical contrast enhancement).

Due to the higher sensitivity of cyst detection, modified Ravine’s criteria are used in diagnosing ADPKD (Table 4). Typical CT and MRI images of kidneys in ADPKD are presented in Figures 2–4.

In case of non-simple cysts, Bosniak’s classification is used for determination of further diagnostic and therapeutic

| Age in years | Number of cysts in both kidneys |
|-------------|----------------------------------|
| <30         | 5 or more                        |
| 30–44       | 6 or more                        |
| 45–59 (women)| >6                               |
| 45–59 (men) | >9                               |

Table 4. Diagnostic criteria for ADPKD in MRI in patients with a positive family history.

Figure 2. MRI scan, T2-weighted. ADPKD – enlarged kidneys with multiple cysts, no normal parenchyma present.

Figure 3. MRI scan, MIP 3D reconstruction. ADPKD – enlarged polycystic disease of markedly enlarged kidneys.

Figure 4. CT scan, contrast-enhanced. ADPKD.
management. Formulated on the basis of CT images, the classification may also be used in the case of MRI scans. Due to the higher selectivity of MRI scans in visualizing compartments and thickening, lesions classified as grade IIF using CT examinations may be classified as grade III following MRI examination.

The necessity for administration of a contrast agent for both CT and MRI scans is associated with risk of renal and nephrogenic complications, occurring particularly in case advanced renal insufficiency and including contrast-induced acute kidney injury (CI-AKI) for CT scans and nephrogenic systemic sclerosis (NSS) for MRI scans; hence the need to follow the recommendations of the Polish Medical Society of Radiology and the European Society of Radiology, provide specialist supervision, and perform laboratory analysis of renal function before scan acquisition. In all patients, the contrast agent should be used in the lowest possible quantity. Despite the fact that patients should not be refused contrast-enhanced examinations in clinically justified situations, alternative and non-burdening imaging methods should be proposed in all cases. Decisions to administer contrast agents to patients at increased risk of adverse effects should be made on a case-by-case basis, with clinical data and expected diagnosis being taken into account.

**Differential Diagnosis**

The main difficulty with diagnostic imaging of ADPKD consists in the fact that the disorder belongs to a wide spectrum of congenital, developmental or acquired cystic kidney diseases. Congenital pathologies include ARPKD, medullary cystic kidney disease, Von Hippel-Lindau syndrome and tuberous sclerosis. Diseases of non-genetic origin include acquired cystic kidney disease (in patients with end-stage renal disease), medullary sponge kidney, multicystic dysplastic kidney and localized renal cystic disease. All these disorders should be taken into account in differential diagnostics of patients with suspected ADPKD. However, many of these disorders are very rare.

**Table 5. Differentiation between cognate cystic renal diseases and ADPKD.**

| Symptomatology of renal lesions | Extrarenal symptoms |
|--------------------------------|---------------------|
| **Medullary cystic kidney disease** [27–29], Figure 5 | Numerous kidneys, usually not larger than 3 cm in diameter at the interface between renal medulla and cortex and within the renal medulla |
| **Von Hippel-Lindau syndrome** [30,31] | Numerous cysts of varied size in slightly more than 50% of patients (59–63%), accompanied by solid lesions (often numerous): RCC |
| **Tuberous sclerosis** [32,33] | Numerous, bilateral renal cysts (in 14–32% of patients) with numerous accompanying angiomyolipoma-type lesions |

**Table 6. Differentiation between acquired cystic renal diseases and ADPKD.**

| Symptomatology of renal lesions | Comments |
|--------------------------------|----------|
| **Acquired cystic kidney disease** [34] | Small kidneys in patients with end-stage renal disease originating from causes other than cystic kidney diseases numerous cysts (3 or more within each kidney) Increased risk of bleeding and RCC development |
| **Medullary sponge kidney (Lenarduzzi-Cacchi-Ricci disease)** [35] | Medullary nephrocalcinosis, numerous tiny cysts within the renal medulla Bilateral location of lesions |
| **Multicystic dysplastic kidney** [1] a few (i.e., cystic renal cell carcinoma, cystic nephroma, cystic partially differentiated nephroblastoma, mixed epithelial and stromal tumor | Non-functioning kidney numerous peripheral cysts with solid lesion in the center Undeveloped or atrophic pyelocalyceal system and renal vessels |
| **Localized renal cystic disease** [36], Figure 6 | A conglomerate of numerous simple cysts of various sizes, interspersed by normal or atrophic renal parenchyma Unilateral lesions contralateral kidney unremarkable, cyst-free |
Radiological symptomatology of cystic kidney diseases is presented in tables (Tables 5, 6) as well as Figures 5, 6.

**Complications**

Image polymorphism is a characteristic feature of cystic kidneys (Figure 7). Cyst complications develop quickly, leading to their abnormal appearance in diagnostic imaging examinations (i.e. different from diagnostic criteria characteristic for simple cysts) (Table 7). Bleeding into the cyst lumen (explained by abnormal cystic wall structure) is relatively common. Cyst infection is the second most common cause of deaths in ADPKD patients. It may be difficult to differentiate between the infection and bleeding into the cyst lumen using ultrasonography, CT, or even MRI. Symptomatology of non-simple cysts is presented in Table 8 as well as Figures 7 and 8. Due to the need to initiate appropriate therapeutic management, diagnosis must be closely correlated with clinical presentation.

Characteristic features of infected cysts in diagnostic images include the presence of fluid/fluid interface, disturbed (restricted) diffusion (increased intensity of signals in DWI-MR images) and wall thickening. According to the new criteria for the diagnosis of infected cysts, at least two of the above conditions should be detected. Gas bubbles may not be visualized in all cases [37].

Differentiation of non-simple cysts from solid focal lesions is a significant diagnostic problem. In CT and MRI, the diagnosis of RCC and other solid lesions (other malignant tumors, metastases and benign solid lesions, such as...
oncocytoma, angiomyolipoma) in ADPKD patients is based on general criteria which usually require contrast administration (Figure 9). When assessing CT examinations, one should keep in mind the contrast-induced pseudo-enhancement of cysts, i.e. the cyst density being increased by 10–20 H.U. after contrast administration. The phenomenon was observed both in phantom studies as well as in vital stains and was found to be dependent on the size of the lesion, the methodology of examination (slice thickness, scanner type (number and size of detectors, reconstruction algorithm)), and the size of the region of interest (ROI). Contrast pseudo-enhancement is observed mainly in small cysts (below 20 mm in diameter) and usually does not exceed 20 H.U. Therefore, pathological attenuation coefficient of at least 20 H.U. should be considered as indicative of pathological contrast enhancement despite the fact that Sai et al. observed an enhancement of more than 20 H.U. in 30% of cases.

### Table 7. Complications of renal cysts in imaging examinations.

| Methodology of examination | US | CT | MRI |
|---------------------------|----|----|-----|
| Wall thickening           | +  | +  | +   |
| Compartments/nodular solid elements | +  | +  | ++  |
| Calcifications in the wall | +  | ++ | –   |
| Thick (high-protein content) | +  | +  |     |
| Fluid/fluid level         | +/-| +  | ++  |

### Table 8. Increased cyst density (bleeding, infection) in diagnostic imaging examinations.

| Methodology of examination | Symptoms |
|---------------------------|----------|
| Ultrasonographic scan     | Non-homogeneous content<br>Echo reflection within the cyst lumen<br>Echo enhancement beyond the posterior wall |
| CT                        | Hyperdensity (above 10 H.U.)<br>Fluid/fluid level |
| MRI                       | Hypointense signals in T2-weighted and DWI (b=0) images<br>Hyperintense signals in T1-weighted images<br>Fluid/fluid level |

**Figure 8.** Multiphase CT scan. Cystic right kidney, status post-left-sided nephrectomy. High protein-content cyst (hyperdense in-phase image without contrast enhancement) — marked with the dark arrow. Normal enhancement of renal parenchyma — marked with the bold arrow.
of simple cysts [38]. At the same time, significantly lower pseudo-enhancement of cysts sized 20–30 and absence of pseudo-enhancement of cysts with diameters larger than 30 mm is observed.

CT scans TK should include the native phase (i.e. before intravenous administration of contrast). In cases when non-enhanced phase is missing, it is advisable to assess the lesion’s radiation attenuation coefficients in two phases following contrast administration (arterial phase and parenchymal phase). Solid kidney lesions (tumors) present with enhancement differences of more than 10 H.U. Hypodense lesions with differences lower than 10 H.U. are most likely thick-content cysts (although tumor can’t be ruled out on the basis of this assessment) [39]. This is all the more complicated due to the different behavior of histopathological subtypes of renal cell carcinoma-RCC in CT studies. The clear-cell subtype (ccRCC) is usually hypervascular in the aortic phase with the contrast agent being washed out in the subsequent phases. The papillary subtype (pRCC) is usually hypovascular and presents with constant or increasing enhancement [40]. Usually, pRCC enhancement is weaker than that of the renal cortex; the enhancement may be so weak that it may be misinterpreted as cyst pseudo-enhancement. In addition, some pRCCs may remain not enhanced and present with cyst-like components. Small regions of interest (ROI) located within the peripheries of the lesion may be helpful in CT differentiation [41].

In MRI, contrast-enhanced T1-weighted sequences are universally considered the diagnostic standard in differentiation of solid lesion (Figure 10). Due to the concomitant renal insufficient, they are often contraindicated in ADPKD patients. Hence, diffusion-weighted imaging (DWI) was attempted (Figure 11). However, no uniform methodology was developed to date with regard to this examination while current recommendations remain ambiguous. Typically, at least two values of the b coefficient are selected: low, i.e. <200 \([s/mm^2]\) and high, i.e. >500 \([s/mm^2]\).
for the purposes of renal imaging, the preferred $b$ value is about 1000 [s/mm$^2$]). In 2014, there were published the results of a meta-analysis that assessed the applicability of DWI in differentiation of focal lesions in kidneys [42]. The authors compared the apparent diffusion coefficient (ADC) values for normal renal parenchyma, cysts, solid benign lesions (including oncocytoma and angiomyolipoma (AML)) to those for malignant lesions (RCC, urinary tract epithelioma) to conclude that lower ADC values may be indicative of malignant lesions. After normal parenchyma and cysts were excluded, the differences obtained from the comparison of ADC values for oncocytoma and AML to those for malignant lesions (RCC) were statistically significant (p<0.0001). In ADC imaging, simple renal cysts present with high signal intensities at low values of $b$; the intensity is reduced for $b>500$ [s/mm$^2$], and wanes...
was observed in 5% [48] to 12% [5] of patients, the role of ADPKD as a risk factor of RCC is still unclear. Due to the absence of epidemiological, clinical, or molecular biology studies that would elucidate the increased incidence of RCC in ADPKD patients, the concomitance of both disorders is considered to be incidental. On the other hand, however, the nature of the disease consists in enlargement and deteriorated function of kidneys leading to end-stage kidney disease and, as a consequence, to long-term dialysis treatment which is an undeniable RCC risk factor [48]. Hence the particular importance of unambiguous differentiation of non-simple cyst from solid tumor lesion, particularly when sparing surgical treatment is possible.

**Diagnostic Imaging of Concomitant Pathologies**

Most important extrarenal symptoms of ADPKD include cystic liver disease and increased incidence of intracranial aneurysms as compared to the overall population (Figure 12). Other symptoms usually have no impact on the course of the disease.

Despite the widely known fact of the incidence of intracranial aneurysms leading to subarachnoid hemorrhages being higher in ADPKD patients (4% to 22.5%), no general guidelines have been established to date with regard to the diagnostics of these patients [49]. Postulates to introduce screening examinations are becoming common, particularly in relation to their importance before the end-stage renal disease as aneurysmal ruptures are common before dialysis treatment is initiated [50,51]. This pertains in particular to patients after the age of 45 with high fluctuations of arterial blood pressure [49]. Intracranial aneurysms in ADPKD patients are detected mainly by angio-MR imaging with time-of-flight (TOF) detection. The method is absolutely safe for patients with renal insufficiency; however, it is characterized by limited sensitivity, particularly with regard to detection of small aneurysms. In addition, false positive results may be obtained. When assessing angiographic examinations, one should be particularly accurate in differentiation between potential fusiform aneurysms

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**Figure 12.** Angio-MRI, TOF. Aneurysm at the bifurcation of the right middle cerebral artery in an ADPKD patient.

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**Figure 13.** MRI scan: (A) FLAIR image; (B) DWI image; (C) T2-weighted image. Middle cranial fossa arachnoid cyst on the left.
and dolichoectasies, more common in this group of patients. In case of ambiguous images, MRI is recommended as second choice, with angio-CT being reserved only for patients whose aneurysms are growing in size [50].

Besides dolichoectasies, cerebral MRI scans in ADPKD patients reveal more common incidence of arachnoid cysts (Figure 13) [51].

Single cysts and polycystic liver disease (PLD) are one of the most common extrarenal manifestations of the disease. PLD is diagnosed when the number of hepatic cysts exceeds 20, both in patients with PKD1 or PKD2 gene mutations as in patients without any defects within these genes [53]. The disease may also be observed without concomitant renal cysts (isolated polycystic liver disease, PCLD). Similar to ADPKD, PCLD is a genetically heterogeneous group of disorders. Two genes of isolated polycystic liver disease, not associated with ADPKD, were identified (PRKCSH and SEC63) [52–54].

Symptomatology of hepatic cysts (Figure 14) in imaging examinations is the same as in the case of renal cysts. Complications of cysts are observed most commonly in patients undergoing dialytic treatment or patients after renal transplants. Most commonly, these include infection, bleeding, or rupture.

In addition, common biliary duct (CBD) should be assessed in detail in hepatic US, CT, or MRI examinations. Asymptomatic dilation of CBD (Figure 15) is observed only in about 40% of ADPKD cases [55].

Symptomatology of other lesions that may accompany ADPKD (e.g. splenic or pancreatic cysts) is typical and affords no special diagnostic difficulties.

**Follow-Up Examinations**

Imaging techniques are used not only for diagnosing the disease and its complications, but also for assessing the disease progression. The assessment of disease progression requires determination of the number and size of cysts as well as the size of kidneys. Although ultrasonography is the method of choice in ADPKD diagnosis, CT and MRI scans are more useful in assessing the disease progression. Limitations of ultrasonography are associated, among other factors, with its dependence on methodology and operator reliability. In addition, ultrasound scanning is ineffective in the assessment of small cysts, smaller than 1 cm in size.

One of the parameters assessed by the imaging examinations when evaluating disease progression is the size of the kidneys expressed by renal volume. In US scans, one may attempt the assessment of kidney size by using the three dimensions (maximum length, width, and posteroanterior dimension) and subsequent calculation of volume using the formula for calculating the volume of rotational ellipsoid. This method underestimates the size of the kidneys (by ca. 25%) as compared to the MRI-based volume assessment [56]. Differences were also observed between the assessment of renal volume in stereological MRI scans and measurements including the three largest dimensions (using the formula for calculating the volume of rotational ellipsoid). The second method also underestimates the renal volume due to various factors including the irregular shape of cystic kidneys, often much different from that of rotational ellipsoid.

Initially, computed tomography was used to estimate the size (volume) of kidneys in ADPKD patients; this was all the more justified, that the accuracy of volumetric measurements is similar for CT and MRI. However, due to the use of ionizing radiation and the use of nephrotoxic contrast agents, the method is markedly worse in long-term follow-up of ADPKD patients. Currently, MRI is considered to be the gold standard in the assessment of renal volume.

As demonstrated by the Consortium of Radiologic Imaging Studies of Polycystic Kidney Disease (CRISP), the size of kidneys is correlated with their efficiency as measured by eGFR [7]. In the study, the total volume of kidneys increased by 5.3% over one year of follow-up. The measurements were used by contrast-enhanced stereological T1-weighted MR images acquired in frontal plane. Due to the risk associated with potential development of nephrogenic systemic fibrosis (NSF), the study protocol was modified so as to...
abandon the contrast-enhancement phase. The increase in renal volume was fasted in patients with faster deterioration of renal function. It was also observed that in patients with total kidney volume (TKV) of above 1500 cm³, eGFR was reduced at the rate of 4.3 ml/min/year [7]. Besides the renal volume measurements, cyst volume measurements were also performed (using T2-weighted images) with the observed increase rate of 12% during a year.

Currently, the assessment of renal volume is made independent of patient’s dimensions (height) by using the ratio of TK to the weight in meters (height-adjusted TKV, htTKV). High risk of disease progression and renal insufficiency was observed in a 8-year follow-up of patients with htTKV ≥600 cm³/m, indicating that htTKV is an important prognostic biomarker [57].

Radiological examinations are useful not only in diagnosing and monitoring the disease progression, but also as a supportive tool in the treatment.

Both hepatic and liver cysts may cause complaints due to their large size and compression of neighboring organs, particularly abdominal or back pain. In persistent complaints, the treatment method of choice includes sclerotherapy with alcohol, performed under ultrasonographic control. A large group of symptoms is caused by bleeding into the cyst or by cyst infection. Symptomatic cysts, particularly infected cysts, are treated by transcunature puncture and aspiration of cyst content under ultrasonographic control. Multiple cysts of liver and kidneys that require treatment are subjected to multi-stage therapy eliminating the need for surgical intervention [58].

Currently, the management of ADPKD patients consists in the treatment of complications within the urinary system (pain, infections), arterial hypertension and renal replacement therapy in the end-stage chronic renal disease. Elucidation of genetic principles and pathomechanisms responsible for the development of cysts contributed to the studies on novel directions in ADPKD treatment aimed at the reduction in the number and size of the cysts and thus at reduction of the total kidney volume. In such cases, MRI provides the best tool for the monitoring of treatment efficacy.

Conclusions

To sum up, the key role of diagnostic imaging methods (ultrasound, CT, and MRI) in the diagnosis and monitoring the progression of ADPKD must be highlighted.

MRI scans are gaining in importance, particularly when used as part of advanced technique protocols. Due to the lack of negative biological consequences, MRI scans may be repeated multiple times which is particularly important in patients at higher risk of RCC or patients after kidney transplants. Volumetric MRI techniques are useful in the assessment of disease progression and the monitoring of treatment efficacy.

References:

1. Truong LD, Choi YJ, Shen SS et al: Renal cystic neoplasms and renal neoplasms associated with cystic renal diseases: Pathogenetic and molecular links. Adv Anat Pathol, 2003; 10(3): 135–59.
2. Bisceglia M, Galliani CA, Senger S et al: Renal cystic diseases: A review. Adv Anat Pathol, 2006; 13(11): 28–66.
3. Rossetti S, Burton S, Strmecki L et al: The position of the polycystic kidney disease 1 (PKD1) gene mutation correlates with the severity of renal disease. J Am Soc Nephrol, 2002; 13(13): 2300–37.
4. Rossetti S, Chauveau D, Kubly V et al: Association of mutation position in polycystic kidney disease 1 (PKD1) gene and development of a vascular phenotype. Lancet, 2003; 361: 2196–201.
5. Torres VE, Harris PC, Pirson Y: Autosomal dominant polycystic kidney disease. Lancet, 2007; 369: 1287–301.
6. Chapman AB, Gusy-Woodford LM, Grantham JJ et al., and CRISP Consortium for Radiologic Imaging Studies of Polycystic Kidney Disease cohort: Renal structure in early autosomal-dominant polycystic kidney disease (ADPKD): The Consortium for Radiologic Imaging Studies of Polycystic Kidney Disease (CRISP) cohort. Kidney Int, 2003; 64: 1035–45.
7. Grantham JJ, Torres VE, Chapman AB et al., and CRISP Imaging Studies of Polycystic Kidney Disease cohort: Renal structure in early autosomal-dominant polycystic kidney disease (ADPKD). J Am Soc Nephrol, 2006; 17: 2098–91.
8. Chapman AB, Johnson A, Gabow PA, Schrier RW: The renin-angiotensin-aldosterone system and autosomal dominant polycystic kidney disease. N Engl J Med, 1998; 323: 1091–96.
9. Torres VE: Water for ADPKD? Probably, yes*. J Am Soc Nephrol, 2006; 17: 2098–91.
10. Wolyniec W, Jankowska MM, Krol E et al: Nowoczesna diagnostyka wielotorbielowatych zwrodnienia nerek typu dorosłych. Pol Arch Med Wewn, 2008; 118: 767–73 [in Polish].
11. Sujansky E, Kreutzer SB, Johnson AM et al: Attitudes of at-risk and affected individuals regarding presymptomatic testing for autosomal dominant polycystic kidney disease. Am J Med Genet, 1993; 35: 510–15.
12. de Rycke M, Georgiou I, Sermon K et al: PGD for autosomal dominant polycystic kidney disease type 1. Mol Hum Reprod, 2005; 11: 65–71.
13. Rossetti S, Strmecki L, Gamble V et al: Mutation analysis of the entire PKD1 gene. Genetic and diagnostic implications. Am J Hum Genet, 2001; 68: 46–63.
14. Nicolai C, Torra R, Badena C et al: Autosomal dominant polycystic kidney disease types 1 and 2: Assessment of US sensitivity for diagnosis. Radiology, 1999; 213: 273–76.
15. Demetriou K, Tziakouri C, Anninos K et al: Autosomal dominant polycystic kidney disease-type 2. Ultrasound, genetic and clinical correlations. Nephrol Dial Transplant, 2000; 15: 205–11.
16. Barua M, Pei Y: Diagnosis of autosomal-dominant polycystic kidney disease: An integrated approach. Semin Nephrol, 2010; 30: 556–65.
17. Gabow PA, Kimberling WJ, Strain JD et al: Utility of ultrasonography in the diagnosis of autosomal dominant polycystic kidney disease in children. J Am Soc Nephrol, 1997; 8: 105–10.
18. Kremer H, Dorhanski W: Diagnostyka ultrasonograficzna, First Edition in Polish. Wrocław: Urban & Partner, 1996 [in Polish].
19. Ramamurthy NK, Moosavi B, McInnes MDF et al: Multiparametric MRI of solid renal masses: Pearls and pitfalls. Clin Radiol, 2015; 70(3): 304–16.
20. Leyendecker JR, Barnes CE, Zagoria RJ: MR urography: Techniques and clinical applications. Radiographics, 2008; 28: 23–46.
21. Neugarten J, Golestaninejad L: Blood oxygenation level-dependent MRI for assessment of renal oxygenation. Int J Nephrol Renov Dis, 2014; 7: 421–35.
22. Pei Y, Hwang YH, Conklin J et al: Imaging-based diagnosis of autosomal dominant polycystic kidney disease. J Am Soc Nephrol, 2015; 26(3): 746–53.
23. Bonniak MA: The current radiological approach to renal cysts. Radiology, 1986; 158: 1–10.
24. Israel GM, Hindman N, Bonniak MA: Evaluation of cystic renal masses: Comparison of CT and MR imaging by using the Bonniak classification system. Radiology, 2004; 231: 365–71.
25. ESUR Guidelines 8.1 Contrast Media Guidelines, http://www.esur.org/esur-guidelines/
26. Katabathina VS, Koga T, Dasyam AK et al: Adult renal cystic disease: A genetic, biological, and developmental primer. Radiographics, 2010; 30(6): 1509–23
27. Hildebrandt F, Otto E: Molecular genetics of nephronophthisis and medullary cystic kidney disease. J Am Soc Nephrol, 2000; 11: 1753–61
28. Rizk D, Chapman AB: Cystic and inherited kidney diseases. Am J Kidney Dis, 2003; 42: 1305–17
29. Meier P, Farres M, Mougnot B et al: Imaging medullary cystic kidney disease with magnetic resonance. Am J Kidney Dis, 2003; 42: 88–10
30. Choyke PL, Glenn GM, Walther MM et al: von Hippel-Lindau disease: Genetic, clinical, and imaging features. Radiology, 1995; 194: 629–42
31. Leung BS, Biswas SV, Duncan M, Rankin S: Imaging features of von Hippel-Lindau disease. Radiographics, 2008; 28: 65–79; quiz 323
32. Rakowski SK, Winterkorn EB, Paul E et al: Renal manifestations of tuberous sclerosis complex: Incidence, prognosis, and predictive factors. Kidney Int, 2006; 70: 1777–82
33. Umeoka S, Koyama T, Miki Y et al: Pictorial review of tuberous sclerosis in various organs. Radiographics, 2008; 28(7): e32
34. Grantham JJ: Acquired cystic kidney disease. Kidney Int, 1991; 40: 143–52
35. Maw AM, Mogibow AJ, Grasso M, Goldfarb DS: Diagnosis of medullary sponge kidney by computed tomographic urography. Am J Kidney Dis, 2007; 50: 146–50
36. Bisciglia M, Creti G: AMR series unilateral (localized) renal cystic disease. Adv Anat Pathol, 2005; 12: 227–32
37. Suwabe T, Ubara Y, Sumida K et al: Clinical features of renal cyst pseudoenhancement on multi-phase CT: Preliminary findings. Eur J Radiol, 2014; 83: 239–44
38. Lassel EA, Rao R, Schwenke C et al: Diffusion-weighted imaging of focal renal lesions: A meta-analysis. Eur Radiol, 2014; 24: 241–49
39. Zagoria RJ, Gasser T, Leyendecker JR et al: Differentiation of renal cell carcinoma and renal cysts on multi-phase CT: Preliminary findings. Eur J Radiol, 2014; 83: 239–44
40. Gaulden MW, Ng Q, Genega EM et al: Renal cell carcinoma: Dynamic contrast-enhanced MR imaging for differentiation of tumor subtypes – correlation with pathologic findings. Radiology, 2009; 250: 793–802
41. Rosenkrantz AB, Matas BW, Portnoy E et al: Impact of size of region-of-interest on differentiation of renal cell carcinoma and renal cysts on multi-phase CT: Preliminary findings. Eur J Radiol, 2014; 83: 239–44
42. Lassel EA, Rao R, Schwenke C et al: Diffusion-weighted imaging of focal renal lesions: A meta-analysis. Eur Radiol, 2014; 24: 241–49
43. Sevenco S, Heinz-Preis G, Ponhold L et al: Utility and limitations of 3-Tesla diffusion-weighted magnetic resonance imaging for differentiation of renal tumors. Eur J Radiol, 2014; 83: 909–13
44. Paudyal B, Paudyal P, Tsushima Y et al: The role of the ADC value in the characterisation of renal carcinoma by diffusion-weighted MRI. Br J Radiol, 2010; 83: 338–43
45. Sandrasegaran K, Sundaram CP, Ramaswamy R et al: Usefulness of diffusion-weighted imaging in the evaluation of renal masses. Am J Roentgenol, 2010; 194: 438–45
46. Squillaci E, Manenti G, Cova M et al: Correlation of diffusion-weighted MR imaging with cellularly of renal tumours. Anticancer Res, 2004; 24: 4175–80
47. Wang H, Cheng L, Zhang X et al: Renal cell carcinoma: Diffusion-weighted MR imaging for subtype differentiation at 3.0 T 1. Radiology, 2010; 257: 135–43
48. Jilg CA, Drendel V, Baier J et al: Autosomal dominant polycystic kidney disease: Prevalence of renal neoplasias in surgical kidney specimens. Nephron Clin Pract, 2013; 123: 13–21
49. Niemczyk M, Pilecki T, Gradzik M et al: Blood pressure and intracranial aneurysms in autosomal dominant polycystic kidney disease. Kidney Blood Press Res, 2014; 39: 630–35
50. Niemczyk M, Gradzik M, Niemczyk S et al: Intracranial aneurysms in autosomal dominant polycystic kidney disease. Am J Neuroradiol, 2013; 34: 1556–59
51. Niemczyk M, Gradzik M, Pęczek L: Arachnoid cyst in autosomal dominant polycystic kidney disease patient. Nephrollogy (Carlton), 2013; 18(11): 745
52. Davila S,uru L, Gharavi AG et al: Mutations in SEC63 cause SECA3 cause autosomal dominant polycystic liver disease. Nat Genet, 2004; 36: 575–77
53. Li A, Davila S, Furu L et al: Mutations in PRKCSH cause isolated autosomal dominant polycystic liver disease. Am J Hum Genet, 2003; 72: 691–703
54. Drent JH, te Morsche RHM, Smink R et al: Germline mutations in PRKCSH are associated with autosomal dominant polycystic liver disease. Kidney Int, 2003; 63: 1439–44
55. Peters DJ, Breuning MH: Autosomal dominant polycystic kidney disease: Modification of disease progression. Lancet, 358: 1439–44
56. Bakker J, Olree M, Kaatee R et al: Comparison of ultrasonography and MRI. Ultrasound Med Biol, 1998; 24: 583–88
57. Chapman AB, Bost JE, Torres VE et al: Kidney volume and functional outcomes in autosomal dominant polycystic kidney disease. Clin J Am Soc Nephrol, 2012; 7: 479–86
58. Lucey BC, Kuliogowska E: Radiologic management of cysts in the abdomen and pelvis. Am J Roentgenol, 2006; 186: 562–73