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Principles of management of patients with autosomal dominant polycystic kidney disease (ADPKD), candidates for kidney and/or liver transplantation — recommendations of the PTT Working Group, part II

ABSTRACT

These guidelines address management of patients with autosomal dominant polycystic kidney disease who are candidates for kidney and/or liver transplantation. The guidelines include such issues as qualifying for transplantation, indications for nephrectomy, indications for simultaneous kidney and liver transplantation, qualification of a living donor, and qualification for renal replacement therapy in patients with a failing transplanted kidney.

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Key words: polycystic kidney disease, polycystic liver disease, chronic kidney disease, transplantation, dialysis

RULES FOR QUALIFICATION OF RELATIVES AS LIVING DONORS

Beata Lipska-Ziętkiewicz, Edyta Szurowska, Joanna Pieńkowska

In typical cases, the first signs of autosomal dominant polycystic kidney disease (ADPKD) develop as late as between 30 and 50 years of age, and, therefore, young hitherto asymptomatic adult family members quite commonly declare their will to donate their kidney to a relative who has already developed end-stage renal disease in the course of ADPKD [1, 2]. Due to the high phenotypic variability of the disease which translates into varying intensity and age-dependence of symptoms, there is a significant risk of ADPKD burden in the relative presenting as a potential candidate for a living organ donor. According to the principles of autosomal inheritance, the risk in first-degree relatives (i.e. children) is as high as 50%; the same pertains to siblings in cases of multigenerational family history of the disease. Therefore, the highest caution is advised when considering relatives as candidates for donation of kidneys to ADPKD patients, and

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any doubt should be interpreted as a contraindication. The candidate should be subjected to a detailed physical examination including assessment of arterial hypertension, which is the earliest clinical manifestation of the disease and which may be revealed already at the developmental age. Subsequently, individuals presenting with no clinical symptoms disqualifying them from becoming donors and/or suggestive of ADPKD (cf. [3]), should be subjected to imaging examinations to exclude morphological changes typical of polycystic kidney disease (PKD); these changes may develop at various ages, but no later than by the age of 40. According to the current position of the Working Group of the Polish Society of Nephrology, magnetic resonance imaging (MRI) is the method of choice [3]. Identification of a total of 10 cysts in a potential high-risk donor aged 16 to 40 years is sufficient to establish the diagnosis of ADPKD while identification of fewer than 5 cysts on an MRI scan is sufficient to exclude the diagnosis of ADPKD (see below, [4]). When no signs suggestive of ADPKD are found in physical and imaging examinations in the relative willing to qualify as a living organ donor, the candidate should be referred to genetic counseling for pedigree analysis and possible qualification for molecular studies before final approval of the candidature. Figure 1 presents a diagram of the process of qualification of relatives willing to become living organ donors for ADPKD patients, including clinical, imaging, and genetic examinations.

RADIOLOGICAL ASPECTS OF QUALIFICATION OF RELATIVES AS LIVING ORGAN DONORS

Joanna Pieńkowska, Edyta Szurowska

Radiological diagnostics plays an important role in the preliminary qualification of potential organ donors. Today, most publications discuss the usefulness of chest radiography (X-ray) screening and abdominal ultrasound screening as methods to assess the general health status of the donor [5]. However, low-dose computed tomography (CT) studies should be used instead in assessment of chest structures as they facilitate more accurate assessment of lungs and the mediastinum at comparable radiation doses (relative to plain radiography). Low-dose CT not only facilitates the exclusion of hyperplastic growth within the lungs, pleura, chest wall, and mediastinum but also assessment of potentially malignant small nodular lesions frequently undetectable in conventional X-ray exams. It is also a method to exclude an acute interstitial or inflammatory process, as well as emphysema, which might be a radiological symptom of chronic obstructive pulmonary disease. The mediastinum is assessed for the presence of enlarged lymph nodes and other hyperplastic lesions within individual compartments. The presence of fluid in the pleural cavity and pericardial sac, the condition of pulmonary vessels, and changes within the visible spine section are also reported. In addition, low-dose CT offers the possibility to assess calcification of coronary arteries (modified Agatston calcium score) as an indicator of the risk of significant stenosis and future coronary events. The absence of calcifications translates to a high likelihood of the absence of significant stenosis within the coronary arteries while a large number of such lesions is an indication for an angio-CT scan of the coronary arteries to assess the significance of lesions and to implement therapeutic procedures. Agatston scores of 0–10 translate into a low risk of significant coronary artery stenosis, whereas the ranges of 11–100, 101–400, and > 400 translate to moderate, moderately high, and high risk of coronary events, respectively.

Conventional ultrasound is the most common modality used for preliminary exclusion of renal cysts due to its high diagnostic accuracy, availability, and low cost. Age-dependent Ravine's criteria are used to evaluate patients with pathogenic variants within the *PKD1* gene (Tab. 1) [6]. In cases presenting with positive family history, the sonographic diagnostic criteria required to confirm the diagnosis include the presence of at least 2 cysts within one or both of the kidneys in persons under the age of 30, at least 2 cysts in each kidney at the age of 30 to 59 years, and at least 3 cysts in each kidney in patients 60 years of age.

Pathogenic variants within the *PKD2* gene are responsible for approximately 15% of all ADPKD cases and are usually associated with a milder form of the disease. In such cases, particularly in young people, Ravine's criteria do not apply due to the risk of false negative results. Thus, unified diagnostic criteria (Table 2) are currently used in screening examinations as they can be used in individuals above the age of 15 presenting with positive family history and any type of mutation [7].

Diagnosis of ADPKD prevents kidney donation. For this reason, a non-invasive method with high diagnostic efficacy [high negative predictive value (NPV) and high specificity]

should be used in imaging of renal cysts. Both of these conditions are met by magnetic resonance imaging which is typically used to evaluate living kidney donors for ADPKD patients at large transplantation centers around the world. The number and nature of cysts can be determined with great certainty non-enhanced MRI (MRI without intravenous contrast media administration) scan due to the high tissue contrast resolution, particularly fluid-containing structures as per the unified ADPKD diagnostic criteria [7]. According to another study, a total of not more than 4 renal cysts is sufficient to exclude ADPKD (NPV 100%, specificity 98.3%) [4]. Molecular studies (cf. below) are required for final determination of candidate status in high-risk individuals under 40 years of age presenting with ambiguous MRI results or no correlation between ultrasound and MRI scans.

When there is no reason to suspect that a kidney donor candidate would develop ADPKD in the future, that is, when the candidate does not meet the unified criteria for ultrasound diagnosis of ADPKD and when not more than 4 cysts have been detected on the MRI scan, a contrast-enhanced abdominal CT scan should be performed [8]. Of course, this examination involves the patient being exposed to ionizing radiation and should be avoided in long-term follow-up; however, it seems that a multi-phase CT scan (non-contrast phase, arterial phase, venous phase, and elimination phase) is necessary before making significant decisions such as that regarding organ procurement.

Computed tomography facilitates not only the exclusion of hyperplastic growth within the abdomen and pelvis minor (not only the urinary tract) but also the anatomical evaluation (size, volume) of kidneys, their possible developmental anomalies (abnormal kidney number, location, shape, or structure, for example, dysplastic kidneys, duplicated pyelocaliceal system), arterial and venous supplies, and excretory function.

Arterial-phase CT scans (angio-CT) are currently the most accurate method of assessment of the number of renal arteries supplying blood to both organs, which may play a decisive role in the choice of the organ to be transplanted. In addition, the location and the distance of renal artery bifurcation relative to its aortic origin should be assessed as it may be important in the planning of renal transplantation. Angio-CT scans also facilitate assessment of the morphology and structure of renal arteries, potential aneurysms, or diseases leading to renal artery stenosis such as fibromuscular dysplasia (FMD), nodular inflammation of arteries, or atherosclerotic lesions constituting contraindications for organ donation [9–11]. The probability of FMD developing in asymptomatic individuals with normal arterial pressure is low and amounts to approximately 5%. In addition, the arterial phase of CT scans is a sensitive modality for the diagnostics of highly vascularized renal tumors such as clear cell renal cell carcinoma, oncocytoma, angiomyolipoma, as well urinary bladder tumors, pancreatic endocrine tumors, primary liver carcinomas, metastatic lesions, etc. It should be kept in mind that more than 50% of renal cancers are incidental findings.

CT scans also allow for exclusion/confirmation of nephro- or ureterolithiasis along with approximate estimation of the chemical composition of stones (calcium or uric acid as based on density); information regarding the absence or presence of lithiasis should be included in the final radiological report.

The non-contrast phase of the CT scan is the most sensitive method for detecting deposits within the ureters, as well as within the pyelocaliceal system and the urinary bladder. It also facilitates detection of complicated (e.g. hemorrhagic) cysts.

The venous phase of the CT scan provides an opportunity for evaluation of the venous system, potential low-vasculature tumors (e.g. chromophobe tumors), as well as cysts, in the aforementioned family donor candidates. Regardless of the previous ultrasound

Table 1. Ravine's criteria for ADPKD diagnosis

Number of cysts		
Age	**Positive family history**	**Negative family history**
< 30 years	≥ 2 in one or both kidneys	> 5 in one or both kidneys
30–59 years	≥ 2 in each kidney	> 5 in each kidney
> 60 years	≥ 3 in each kidney	> 8 in each kidney

Table 2. Uniform diagnostic criteria for ADPKD diagnosis

Confirmation		Exclusion	
Age	**Number of cysts**	**Age**	**Number of cysts**
15–39 years	≥ 3 in one or both kidneys (total)	15–39 years	Non-diagnostic
40–59 years	≥ 2 in each kidney	≥ 40 years	< 2 in each kidney
> 60 years	≥ 4 in each kidney		

scan, the assessment of potential PKD in the venous phase of the supportive and complementary CT scan should be based on the unified criteria for the diagnosis of ADPKD. In cases of discrepancies between CT and US scans when making a decision to qualify a candidate as a kidney donor, the CT scan should be reevaluated. If any ambiguity remains after reevaluation, an MRI scan without contrast enhancement should be acquired [12].

The elimination phase of the CT scan provides information on renal function (confirmation of results obtained in laboratory tests — GFR value, creatinine concentration), visualization of the developmental variants of renal pelvis and ureters (e.g. duplication), developmental defects of the excretory system such as pelviureteric junction stenosis, and evaluation of possible hyperplastic lesions within the renal pelvis, ureters, and urinary bladder. Computed tomography is an accurate method for verification of blood clots, urothelial cancer, or other bladder tumors within the urinary system.

Of course, MRI is also useful in assessment of potential living donors before transplantation; however, one should keep in mind that in-depth evaluation of renal anatomy and function requires intravenous administration of a gadolinium contrast agent. MRI diagnostics is characterized by lower spatial resolution, e.g. in the assessment of additional arterial vessels, which is important in deciding which organ to procure and detecting the presence of translucent deposits within the urinary tract [13, 14]. Therefore, we believe that the CT scan remains the reference diagnostic method in qualification of candidates for organ donation despite ionizing radiation and potential nephrotoxicity associated with the administration of iodinated contrast media. Multiplanar processing and 3D formatting of images without the loss of high resolution are crucial for evaluation and measurement of both anatomical structures and pathologies in potential donors subjected to CT examination.

Ultrasound follow-up scans are recommended every 1–2 years to monitor the health of subjects who have donated one of their kidneys. Modalities that do not involve ionizing radiation, such as ultrasound imaging and MRI as the second-choice method, used in ambiguous cases, are preferred in these subjects. Ultrasound imaging should remain the first-choice modality, and a follow-up scan should be acquired as soon as in the perioperative period to exclude postoperative complications such as hematomas within the resected kidney bed.

SUMMARY

In a relative considered as a potential kidney donor to an ADPKD patient, excluding the risk of the future development of the disease in the donor himself/herself is one of the most important issues. Initial assessment includes an ultrasound examination, and ADPKD diagnosis is then confirmed or excluded on the basis of non-contrast-enhanced MRI scans. These examinations may complete the qualification procedure if the donor candidate meets the diagnostic criteria of ADPKD, and any further proceeding towards organ procurement is thus refused. In cases of a negative result of the MRI ADPKD screening scan, a low-dose chest CT scan with extension to the abdomen and pelvis should be acquired in non-contrast, arterial, venous, and elimination phases. The qualification process for potential donors is shown in Figure 3.

GENETIC ASPECTS OF QUALIFICATION OF RELATIVES AS LIVING ORGAN DONORS

Beata Lipska-Ziętkiewicz

Molecular diagnosis carried out by a specialist in clinical genetics as part of genetic counseling facilitates investigation of variable expression or age-dependent penetrance, so they can be addressed simultaneously with the assessment of disease risk in other family members. In addition, given the predictive nature of the examination carried out in candidates for organ donation, it is also important that consultation also addresses the psychological and social aspects related to the possible diagnosis of ADPKD in an asymptomatic young adult [15].

According to most of the current international and Polish guidelines, routine molecular diagnostics is not recommended when clinical suspicion of ADPKD is made in a subject [3, 16]. The final diagnosis can be determined solely based on clinical criteria based on family history and imaging studies. However, one of three exceptions listed in the Polish Society of Nephrology (PTN) recommendations is related to qualification of relatives as potential candidates for living organ donation; the other two are reproduction counseling and cases requiring differential diagnosis due to unusual clinical presentation (early onset, rapid pro-

gression, and/or negative family history). It should also be stressed that the issue of molecular testing in ADPKD is currently a matter of major dispute, and it is likely that the list of indications will be extended in the near future [17]. Over the past 5 years, in addition to the breakthrough in the availability of next-generation sequencing (NGS), including exome sequencing (ES, aka whole-exome sequencing, WES), first attempts were made at targeted treatment using vasopressin V2 receptor antagonists (tolvaptan). Progress in knowledge is reflected in the latest European guidelines developed by the European ERA-EDTA Working Group for Inherited Kidney Diseases (WGIKD) and the Molecular Diagnostics Tasks of the European Rare Kidney Disease Reference Network (ERKNet) 2021 [18]. According to these guidelines, routine molecular diagnostics is recommended for each patient presenting with a suspected genetically conditioned polycystic disease.

Unfortunately, reliable molecular tests for ADPKD are at present poorly accessible in Poland. This is mainly due to problems with the specific sequence of the *PKD1* gene, which makes the usual molecular techniques (i.e. standard Sanger sequencing and NGS, including ES) perform rather poorly in terms of the detection rate of pathogenic variants in a region overlapping the pseudogene sequence (28–50%), as well as a false-positive rate of about 10% [2, 18]. Reliable genetic tests are difficult to carry out and should be commissioned only in certified diagnostic centers making use of appropriate molecular techniques ensuring long DNA fragment readings. Concerning the above, it is also important that molecular diagnostic tests be started with the recipient so that the exact molecular background of the disease may be determined. However, one should remember that the available methods fail in identifying mutations within the *PKD1* and *PKD2* genes in families meeting the clinical criteria for the disease in as many as 9% of cases [19]. There is, therefore, a risk that the recipient's molecular test will be negative even though the clinical criteria of the disease have been met. In such cases, molecular testing of potential donors will be unjustified. If a pathogenic variant is detected within the *PKD1* or *PKD2* genes in the recipient, a test targeting a particular mutation in the potential donor should be performed as the next step. The result of this test shall be conclusive.

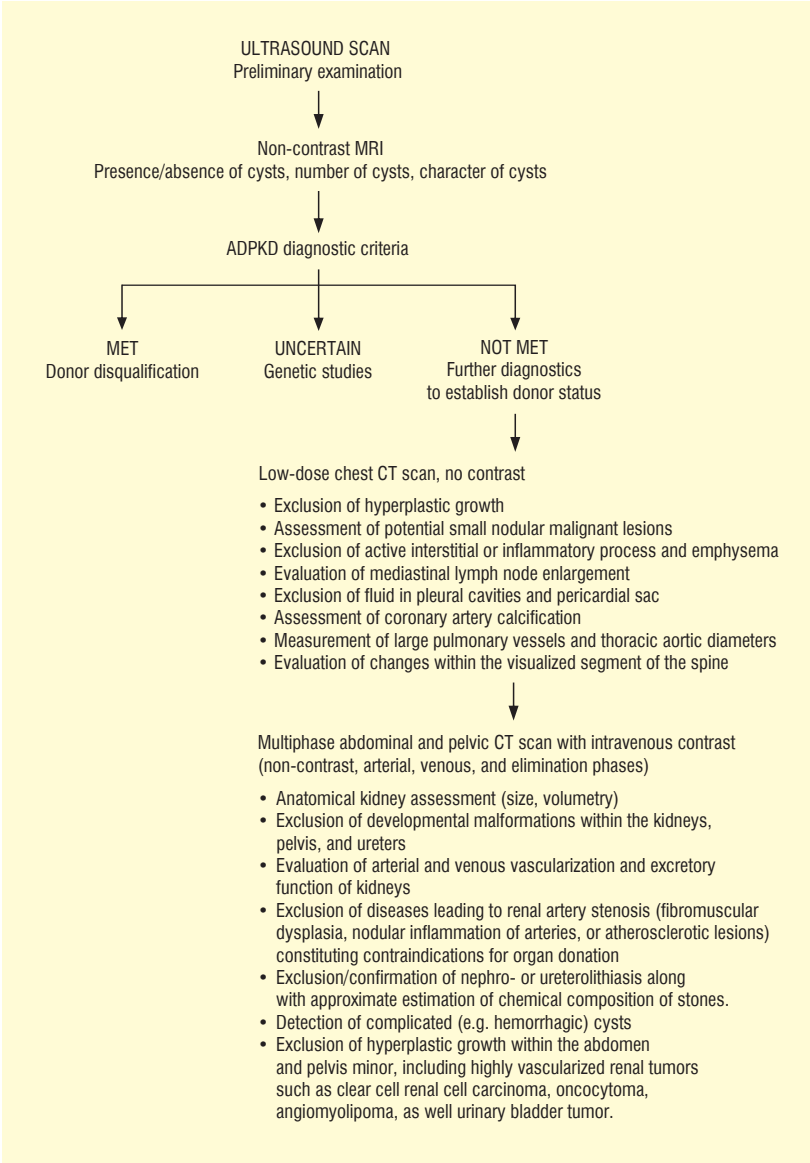

Figure 1. Diagnostic imaging in potential living kidney donors related to ADPKD recipients

SUMMARY

Due to limited access to reliable molecular diagnostic tests and the need to perform these tests in both the recipient and the donor candidate, qualification of the ADPKD patient's relatives as potential kidney donors is a tedious and time-consuming process. It is also associated with the risk of making diagnosis in a person hitherto unaware of his or her illness, which may lead to certain psychological, as well as social, consequences. Therefore, caution should be exercised when presenting this option to ADPKD patients qualified for renal replacement therapy.

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RADIOLOGICAL EVALUATION OF PATIENTS WITH ADPKD BEFORE QUALIFICATION FOR KIDNEY AND/OR LIVER TRANSPLANTATION

Ewa Banach-Ambroziak, Edyta Szurowska

RADIOLOGICAL ASSESSMENT OF KIDNEYS

Kidney size measurement

The significance of height-adjusted total kidney volume (htTKV)

According to the Consortium for Radiological Imaging Studies of Polycystic Kidney Disease (CRISP), the height-adjusted total kidney volume (htTKV) is the most accurate radiographic biomarker used to assess the stage and risk of progression of renal failure in patients with the typical ADPKD variant [1].

Researchers from the Mayo Clinic made use of the htTKV parameter calculated from CT or MRI studies as a basis for a classification that facilitates prediction of the rate of disease progression and thus helps to identify a subgroup of patients at risk of early development of the end-stage renal disease [2]. The classification is available as an online tool [3].

Renal imaging, preferentially with CT or MRI, should be a part of the initial assessment of patients with ADPKD. Radiological re-examination is used in the diagnostics of disease complications, monitoring of the effects of pharmacological treatment, and, increasingly in pretransplantation assessments.

TKV MEASUREMENTS IN INDIVIDUAL RADIOLOGICAL MODALITIES

TKV can be measured from ultrasound, CT, and MRI scans. Ultrasound-based evaluation is not applicable in clinical programs and in monitoring of effects of pharmacological treatment, whereas it is useful in long-term evaluation. Ultrasound assessments are strongly dependent on investigator skill, are less reproducible, and significantly overestimate TKV as compared to CT and MRI [4]. The accuracy of ultrasound-based measurements is inversely proportional to renal enlargement.

CT and MRI provide comparable TKV measurement results; in both cases, no intravenous contrast is required. The disadvantage of CT consists in the patient being exposed to ionizing radiation, which excludes the use of this method in repetitive assessments. T2-weighted magnetic resonance imaging is the modality of choice. MRI does not involve ionizing radiation; however, it is less accessible, more time-consuming, more expensive, and less tolerated.

TECHNIQUES FOR TKV MEASUREMENT

An accurate TKV measurement is necessary to evaluate the impact of treatment interventions and should be performed on the basis of a CT or MRI examination using planimetry or stereology.

In daily clinical practice, faster methods facilitating estimation of the TKV value, are, for example, the ellipsoid volume formula. Discussed below are these two measurement methods with low technical requirements facilitating their widespread use.

1. **Planimetry**

Planimetry is considered to be the reference method characterized by the greatest accuracy and reproducibility. The analysis of a single study lasts 35 to 55 minutes, which limits the possibility of using the method in clinical practice [5]. Using planimetry, the contours of the kidney are manually traced on each cross-section of the test, and the obtained surface areas are automatically summed up, and then multiplied by the thickness of the test layer gives the volume of the kidney (Fig. 2, 3).

Appropriate algorithms available in commercial radiological software facilitate interpolation of part of the data which reduces the measurement time without affecting accuracy of data.

2. **Estimation of TKV based on the ellipsoid volume formula** (Fig. 4.)

The accuracy of TKV estimation using the ellipsoid volume formula is lower than that of

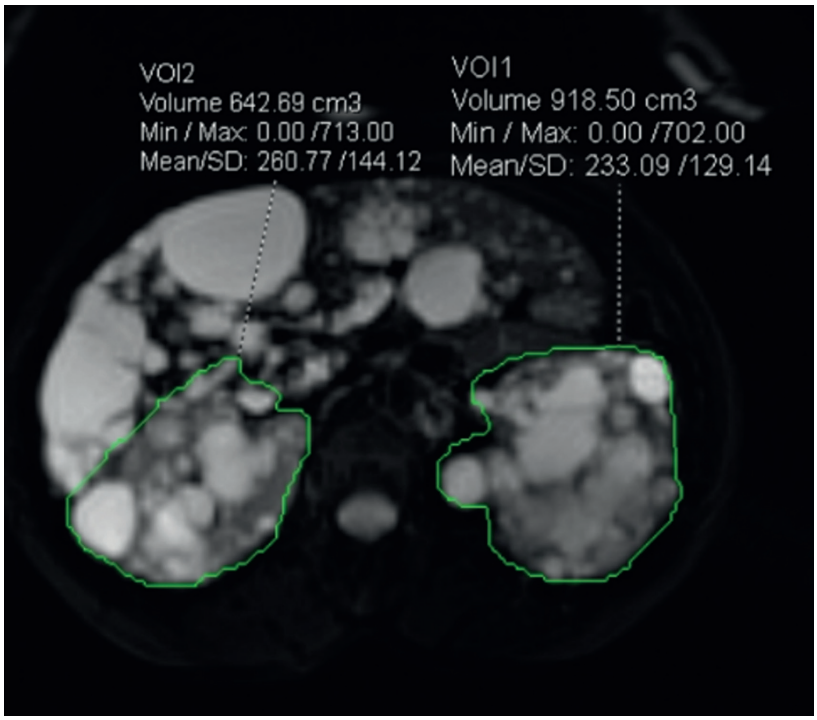

Figure 2. Transverse MRI scan, T2-weighted fat-saturated sequence with renal contours marked

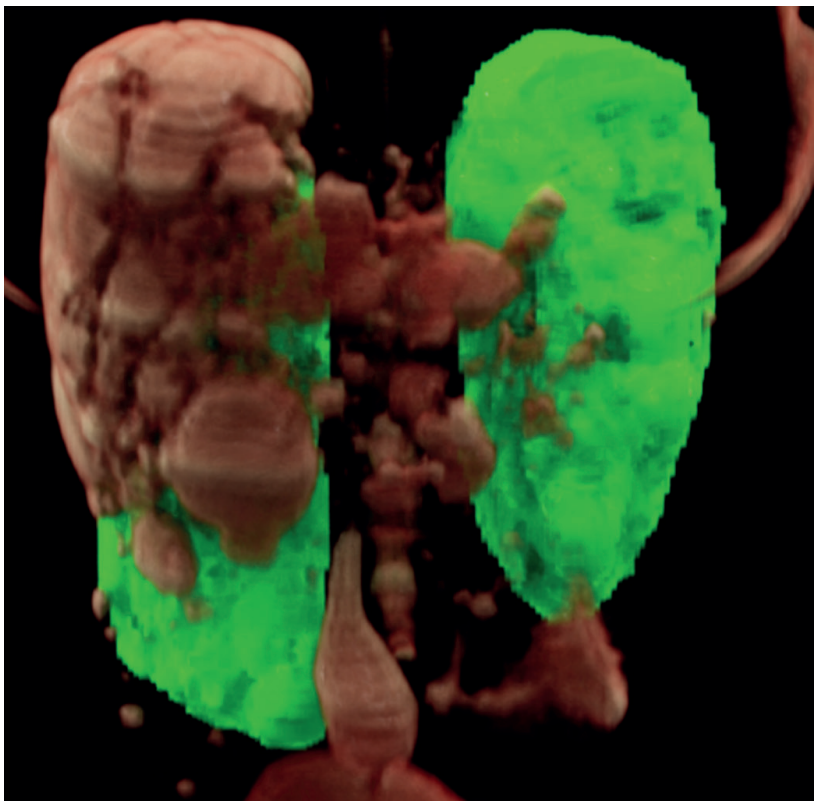

Figure 3. Volume-rendered CT exam

$$eTKV = \frac{\frac{\pi}{6} \times (\text{Length}_{coronal} + \text{Length}_{sagittal})}{2 \times \text{Width} \times \text{Depth}}.$$

Figure 4. Ellipsoid volume formula

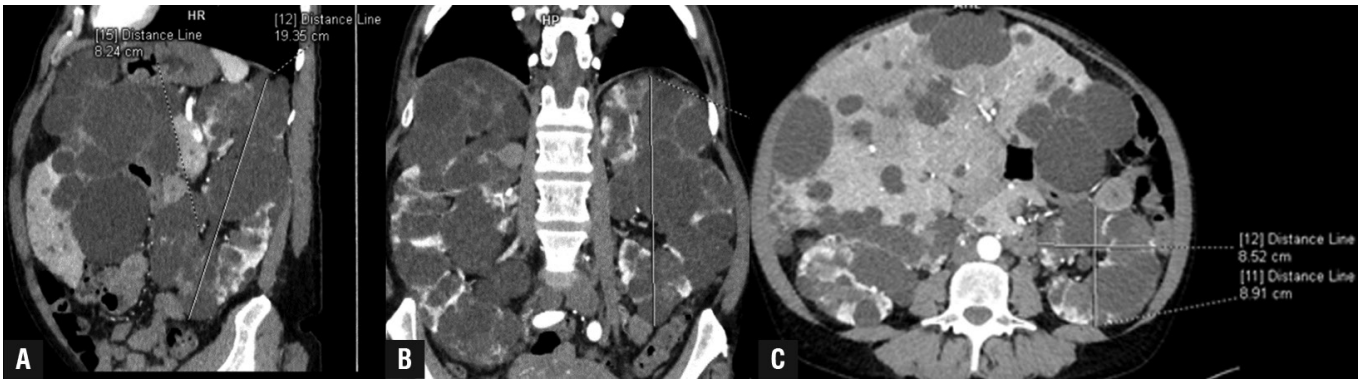

Figure 5. Abdominal CT scans in arterial phase: **A.** kidney length in the sagittal plane; **B.** kidney length in the frontal plane; **C.** kidney width and thickness in the transverse plane

the planimetric method yet sufficient for daily clinical procedures [5]. TKV values obtained using this method can be used to assess the stage and rate of disease progression as per the Mayo classification [2]. The calculation of TKV takes only about 7 minutes and requires the kidney to be measured in three different planes (Fig. 5).

3. **Other measurement methods:** mid-slice method, stereology, semi-automatic/automatic method.

RADIOLOGICAL ASSESSMENT OF RENAL COMPLICATIONS

Evaluation of complicated cysts: post-hemorrhagic cysts with infected contents.

In most cases, intracystic hemorrhage and infection of renal or hepatic cysts can be differentiated from clinical symptoms and laboratory investigation results. Radiological examination is indicated in the event of unclear, deteriorating clinical conditions, increasing inflammatory parameters, or failure of empirical treatment.

ULTRASOUND IMAGING

Preliminary assessment

Ultrasound presentation of a complicated cyst: cyst with echogenic, frequently sedimenting contents, with no internal flows in vascular modes. Infection of the cystic contents may be manifested by the thickening and increased vascular flow within the cystic wall, and the presence of gas and fluid levels in the cyst lumen. Ultrasound imaging is of limited diagnostic capability in moderate to severe cystic remodeling of kidneys and/or liver. Due to the ultrasound penetration depth, parts of the organs may not be available for evaluation.

It is difficult to unambiguously distinguish between a fresh hemorrhagic cyst or an acutely inflamed cyst from a complicated chronic lesion on the basis of ultrasound examinations. The pathognomonic symptom of infection, namely the presence of gas bubbles within the cystic lumen is observed rarely and only in late stages of infection.

Cystic wall thickening may be due to infection, the presence of a paramural clot, or partial contraction of cystic walls following spontaneous lesion rupture.

Targeted ultrasound examination can be used to perform a puncture biopsy with aspiration of the infected contents, following preliminary determination of the infectious focus on CT/MRI or positron emission tomography-computed tomography (PET-CT) scans.

COMPUTED TOMOGRAPHY

Preliminary assessment

CT presentation of complicated cyst: cyst with hyperdense contents, not significantly enhancing after contrast administration, may feature paramural clots and calcifications. Infection of the cystic contents may be manifested by thickening and contrast enhancement of the cystic wall, the presence of gas and fluid levels in the cyst lumen, as well as blurring of the adipose tissue adjacent to the infectious focus. Renal insufficiency greatly restricts applicability of iodinated contrast media.

CT presentations of chronic hemorrhagic cysts and inflammatory cysts may be difficult to distinguish, particularly in scans acquired without contrast media.

An advantage of CT scans consists in the ability to simultaneously assess the remaining organs within the abdominal cavity and pelvis minor, as well as to exclude any extrarenal causes of symptoms (e.g. gallbladder inflammation, choledocholithiasis, nephro-/ureterolithiasis). CT is very effective in the diagnostics of nephro- and ureterolithiasis.

MAGNETIC RESONANCE IMAGING

In-depth evaluation when ultrasound/CT scans are inconclusive

MRI presentation of complicated cyst: Hemorrhagic/high protein cysts typically present with high intensity in T1-weighted images and low-intensity signal in T2-weighted images, as well as diffusion restriction in diffusion-weighted imaging (DWI) sequences and apparent diffusion coefficient (ADC) maps (Fig. 6).

Suwabe et al. found the presence of gas to be pathognomonic for infection, albeit it occurs in only 1.1% of patients. High signal intensity in DWI scans was associated with sensitivity of 86.4% and low specificity of only about 33.3%. Specificity and sensitivity of fluid levels within the cystic lumen, as well as of thickening of cystic walls, were about 80% [6].

The use of intravenous gadolinium contrast is limited due to the risk of developing nephrogenic systemic fibrosis (NSF).

Positron emission tomography with computed tomography

PET-CT is the most sensitive method for diagnostics of renal or hepatic cyst infections [7]. It is useful in cases of diagnostic difficulties encountered in CT/MRI-based assessments. It is the modality of choice facilitating the precise location of cyst infection. However, it is poorly accessible and expensive.

ASSESSMENT OF FOCAL LESIONS WITHIN THE KIDNEYS

The incidence of clinically significant renal cell carcinomas (RCCs) in patients with renal insufficiency in the natural history of ADPKD does not appear to be greater compared to patients with other etiologies of renal failure [8], albeit more recent studies showed that RCC occurred in 5 to 8% of patients with ADPKD. Most lesions were ≤ 2 cm in diameter [9].

SUMMARY OF THE CURRENT RECOMMENDATIONS

- KDIGO 2020: general recommendation regarding the broad population of candidates for a kidney transplant. Ultrasound scanning towards RCC is recommended only in high-risk patients such as those with ≥ 3 years of dialysis therapy, a family history of renal carcinoma, acquired renal cystic disease, or analgesic nephropathy [10].

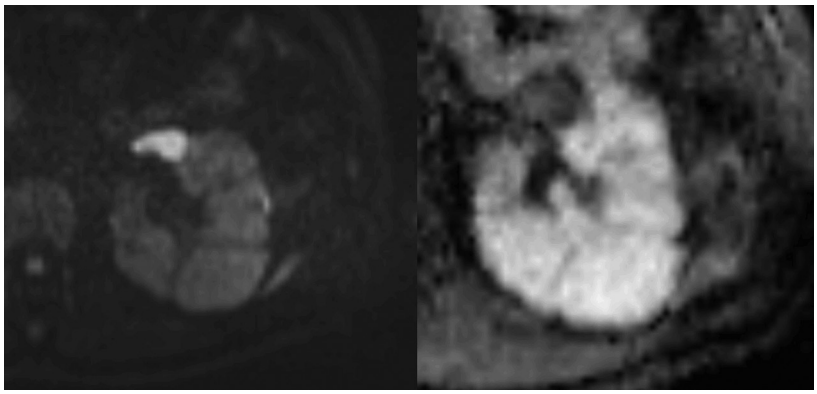

Figure 6. Features of free diffusion restriction on a DWI scan (b-value of 800) and an ADC map

- KDIGO 2015: imaging studies to exclude renal hyperplasia are recommended if no spontaneous resolution of macroscopic hematuria or intracystic bleeding is observed within 2 to 7 days [11].
- Spanish recommendations:
  - if macroscopic hematuria persists for more than one week or if the first episode of hematuria occurs in a patient aged > 50 years, an imaging study is recommended to exclude renal carcinoma;
  - renal carcinoma should be suspected upon the presence of a solid lesion on an ultrasound imaging scan, the presence of non-homogeneous calcifications on a CT scan, focal contrast enhancement, tumor embolus, or regional lymphadenopathy on a CT/MRI scan [12].

RADIOLOGICAL ASSESSMENT OF LIVER

Liver cysts are observed in more than 80% of adults with ADPKD [13]. Cystic remodeling of the liver tends to progress with age. Cysts are more prevalent in female patients, particularly in multiparous mothers and women receiving exogenous estrogens.

Most patients with the diagnosis of PLD (*polycystic liver disease*) experience no symptoms, and liver function remains uncompromised even in advanced PLD. However, approximately 20% of patients with extreme PLD report symptoms suggestive of abdominal compartment syndrome, such as epigastric fullness, early postprandial satiety, abdominal pain, lumbar pain, or gastroesophageal reflux symptoms [14]. In such cases, therapeutic management should be initiated, its final stage consisting of liver transplantation.

PLD DIAGNOSTIC CRITERIA

Initial assessment of a patient with ADPKD should include liver imaging to assess the severity of PLD. The diagnosis of PLD requires at least 20 cysts to be visualized in the liver in ultrasound examination.

PLD SEVERITY ASSESSMENT

The liver size is most accurately represented by the height-adjusted total liver volume (ht-TLV). Volumetric measurement can be performed on CT or MRI scans using basic radiology software tools.

Two classifications are used to evaluate liver enlargement in the course of PLD:

— the classification by Hogan et al. (HALT trials): mild — ht-TLV < 1000 mL/m, moderate – ht-TLV 1000–1800 mL/m, severe – ht-TLV > 1800 mL/m [15];

— the classification by Kim et al.: mild — ht-TLV < 1600 mL/m, moderate: ht-TLV 1600–3200 mL/m, severe: ht-TLV > 3200 mL/m [16]. According to the *Journal of Hepatology* (2018), Kim's classification better corresponds to the severity of symptoms and the need to intensify treatment [17].

The severity of PLD may also be assessed on the basis of Gigot or Schnelldorfer classifications requiring the use of iodinated contrast media (Tab. 2, Fig. 7) [18, 19].

DIAGNOSTICS OF COMPLICATIONS IN THE COURSE OF PLD

In 5% of patients, intracystic bleeding or infection of hepatic cyst is diagnosed; both complications cause acute abdominal pain and require management similar to that followed in similar complications in the kidneys. The radiological image of complicated cysts is identical for renal and hepatic lesions and has been discussed earlier.

SUMMARY OF THE CURRENT RECOMMENDATIONS

- KDIGO: PET-CT is the most sensitive method for the diagnostics of renal or hepatic cyst infections [7, 11].
- Spanish recommendations: CT scan is recommended in case of suspected hepatic cyst infection. Antibiotic treatment must be started immediately (a quinolone antibiotic should be administered over at least 6 weeks, and third-generation cephalosporin should be added if fever persists after 72 hours). When symptoms of infection persist after 3 to 5 days after initiation of antibiotic therapy and CT and MRI results are not conclusive, a PET-CT scan should be acquired using fluorodeoxyglucose (FDG-PET-CT) to accurately locate the infection focus. Percutaneous drainage may be indicated if the infection persists, and the causal cyst has been located and is available for intervention.

Cystic hemorrhage is identified on MRI, and treatment is based on non-opioid and opioid analgesics and rest [12].

RADIOLOGICAL ASSESSMENT OF INDICATIONS FOR NATIVE NEPHRECTOMY

The following considerations focus on radiological assessment of indications for the procedure while a general discussion on indications for nephrectomy has been presented earlier.

Some patients with ADPKD require special management during the peritransplantation period due to the presence of massive cystically remodeled kidneys in the abdominal cavity. Native nephrectomy (NNx) is required in as many as nearly 40% of patients in this group [20, 21].

Qualification for NNx is a significant clinical problem as nephrectomy is associated with significant peri- and intraoperative risks, including the risk of massive blood loss. The transfer of blood products may lead to alloimmunization (*autotransfusion in nephrectomy candidates*). On the other hand, failure to perform nephrectomy in these cases may result in generalized infection or exacerbation of symptoms due to abdominal compartment syndrome.

Qualification for the procedure is based mainly on clinical data. The patient must be assessed by a multispecialty team consisting of a nephrologist, transplant surgeon, general surgeon, and radiologist. The eligibility criteria are subjective and based on the site's experience. However, diagnostic imaging methods, mainly CT and MRI, are increasingly used to objectify indications for the procedure.

SPECIFIC OBJECTIVES FOR IMAGING EVALUATION OF ADPKD PATIENTS BEFORE THE TRANSPLANTATION PROCEDURE

1. Assessment of graft implantation site:
- renal dimensions, TKV;
- identification of the kidney descending lower into the pelvis minor;
- determination whether the kidneys/renal cysts significantly impress the adjacent organs or vascular structures;

Table 2. Gigot classification of PLD severity [18]

Gigot classification	Number of cysts	Size of the cysts	Cyst-free parenchyma area
Type I	< 10	Large (> 10 cm)	Significant
Type II	Numerous	Small, medium-sized	Significant
Type III	Numerous	Small, medium-sized	Insignificant

- craniocaudal (CC) and anteroposterior (AP) dimensions of the liver;
- in cases of concomitant PLD, estimation of TLV and disease severity according to the Gigot/Schnelldorfer classification;
- other: screening for significant scoliosis, abdominal aortic aneurysm, and enlargement of the remaining abdominal and pelvic organs (e.g. spleen, uterus) (Fig. 8).

2. Assessment of renal complications: renal cyst infection, renal cyst bleeding, nephro- and ureterolithiasis, or presence of solid renal lesions.
3. Assessment of vascular access within the iliac axis vessels or alternative vascular access (e.g. distal abdominal aorta, inferior vena cava).
4. Assessment of the presence of significant extrarenal pathologies with particular focus on lesions of suspected hyperplastic character.

RADIOLOGICAL ASSESSMENT OF CEREBRAL VESSELS

The section titled "Other dilemmas regarding the qualification of ADPKD patients. Aneurysms, colonic diverticulosis, and hernias" discusses issues related to occurrence of aneurysms in ADPKD patients and indications for relevant diagnostic examinations; the discussion that follows is focused on radiological diagnostics.

Angio-MRI employing the time-of-flight (TOF) sequence is the method of choice in screening of cerebral vessels as no intravenous contrast medium is required for the imaging (Fig. 9, 10). In cases of contraindications for MRI (e.g., intracerebral ferromagnetic aneurysm clip), or if the modality is not available, angio-CT with iodinated contrast media is used as an alternative.

SUMMARY

CT or MRI are increasingly used as diagnostic imaging techniques used for qualification of ADPKD patients for kidney and/or liver transplantation.

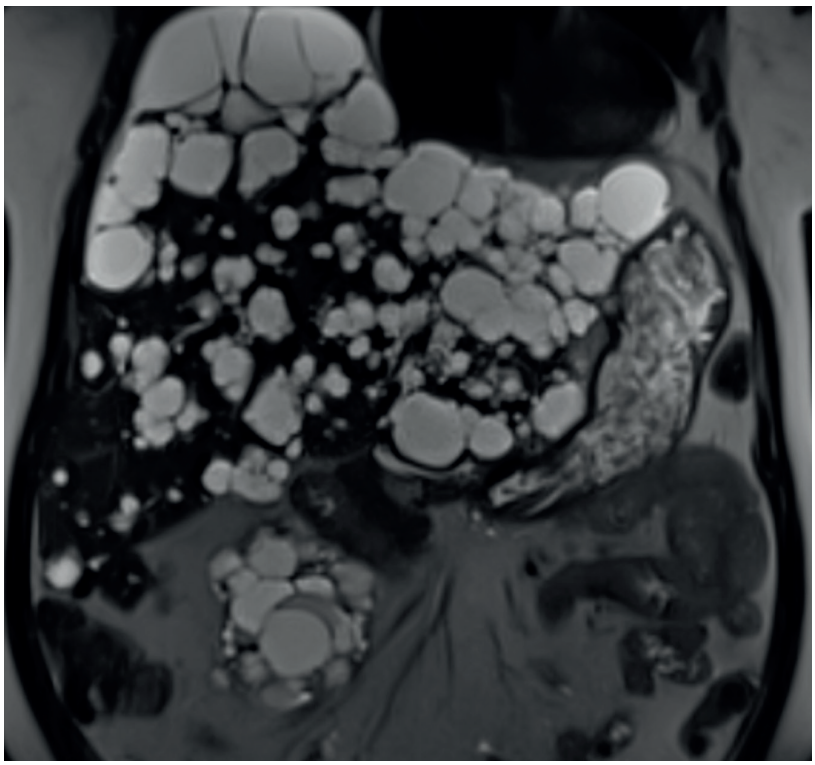

Figure 7. Frontal-plane T2-weighted MRI scan, Gigot stage III PLD

Objectification of indications for native nephrectomy is one of the main objectives of imaging. In addition, imaging studies are used to assess the presence and severity of concomitant polycystic liver disease, as well as the presence of renal and possibly also hepatic complications. The objective of the analysis of the morphology and the course of the iliac vessels, aorta, and inferior vena cava consists in selecting optimum vascular access. In typical conditions, the vascular system is accessed from the iliac axis while alternative vascular access is provided in atypical cases, such as those of anatomical variations, for example, by distal sections of the abdominal aorta or inferior vena cava. Exclusion of hyperplastic lesions within the kidneys or liver or any significant pathologies of other abdominal and pelvic organs is also required. In candidates at high risk of intracranial aneurysm, screening of vessels is recommended, preferentially

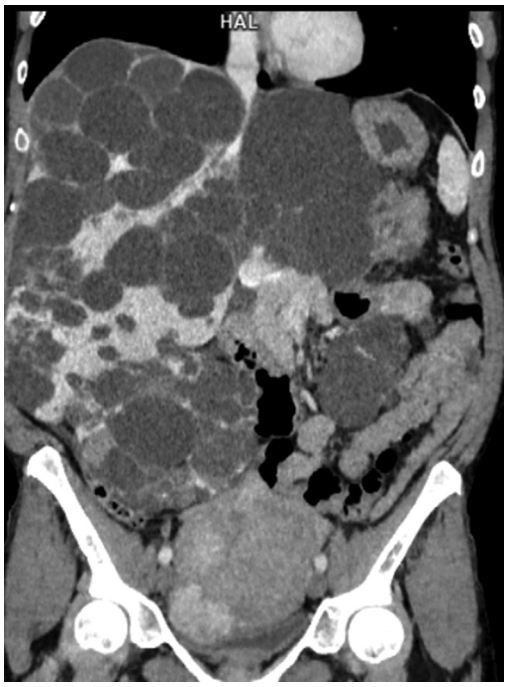

Figure 8. Coronal CT scan in the venous phase. Massive liver and kidney enlargement, significant uterine body enlargement (myomatous uterus)

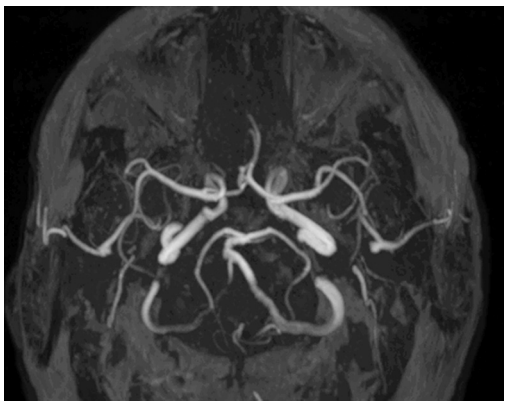

Figure 9. Angio-MRI (TOF), maximum intensity projection (MIP) reconstruction, circle of Willis

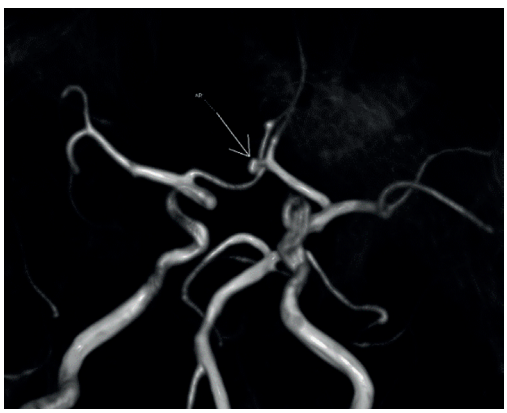

Figure 10. Angio-MRI (TOF), volume rendering, the arrow pointing to an aneurysm of the anterior communicating artery

using time-of-flight angio-MRI (without intravenous contrast administration). In all candidates, a low-dose CT scan should be acquired instead of the diagnostically less informative plain chest X-ray to exclude significant lung and pleural pathologies.

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LONG-TERM CARE TO ADPKD TRANSPLANT RECIPIENTS. QUALIFICATION FOR RETRANSPLANTATION

Magdalena Durlik, Alicja Dębska-Ślizień, Andrzej Oko

Patients with ADPKD are subject to post-transplantation immunosuppressive treatment according to the same rules as those applying to recipients with end-stage renal failure of other etiologies. The choice of immunosuppressive treatment regimen should be guided first by the recipient's immunological risk and then by individual indications/contraindications [1, 2]. The most common regimens include combinations of calcineurin inhibitors (tacrolimus, less frequently cyclosporin A) with mycophenolic acid [mycophenolate mofetil (MMF) or sodium mycophenolate (MPS)] and glucocorticosteroids. Conventional tacrolimus, administered twice a day, may be replaced by an extended-release formulation administered once a day. Calcineurin inhibitors are rarely combined with mTOR kinase inhibitors (sirolimus or the more novel everolimus). Although mTOR inhibitors have the potential to limit the growth of the cysts, they are not recommended as the drugs of first choice because calcineurin inhibitors are crucial to maintaining good graft function. Induction treatment consists of anti-thymocyte sera (thymoglobulin or grafalon) in high-risk patients and basiliximab in the moderate-risk patient. ADPKD patients are characterized by low immunization with no immune response disorders associated with autoimmune disease or previous immunosuppressive therapy; they also rarely require blood transfusion. It is advisable to customize the treatment depending on the immunological risk, concomitant existing diseases, renal function, and possible complications. Within the first 3 to 6 months, immunosuppression should be focused on effectively preventing rejection; after this time, treatment customization should be aimed at maintaining good transplant function for as long as possible.

In the case of simultaneous liver-kidney transplant (SLKP), the liver exerts an immunoprotective effect and lowers the risk of kidney rejection [3, 4]. The protective effect is related to absorption of preformed donor-specific antibodies (DSAs) by the hepatic reticuloendothelial system. SLKP is usually performed based on blood type compatibility without crossmatching or the recipient's immunization level being taken into account; however, no rejection is observed for positive crossmatching results. Reduction of DSA levels (particularly Class I DSAs) has been described. No effect of this type is observed in cases of simultaneous transplants of kidneys and liver recipients. Delayed graft function (DGF) is an adverse event after SLKT; it is recommended to defer the

administration of the calcineurin inhibitor (by 2 days) and initiate the induction treatment with basiliximab in patients at risk.

Comprehensive care provided to recipients of kidney grafts due to ADPKD does not differ from standard post-transplant care and consists of:

- optimization and individualization of immunosuppressive treatment;
- graft function monitoring;
- early detection and treatment of complications;
- prevention of complications;
- patient education.

In clinical practice, graft function monitoring is based on simple biochemical and histological parameters such as:

- eGFR value, serum creatinine level;
- proteinuria;
- biopsy: per protocol or as indicated
- Evaluation: MS (light microscope), ME (electron microscope), IFL (immunofluorescence), C4d deposits, SV40 antigen in renal tissue for *Polyoma BK* infection
- biomarkers: DSA, other — donor-derived cell-free DNA

Patients with ADPKD account for 12 to 15% of renal graft recipients per year. Literature data indicate that patient and graft survival in ADPKD patients is better than in patients without ADPKD. Better survival of graft is affected by the lack of recurrence of native kidney disease. Better patient survival should be attributed to lower co-morbidity. DGF is also reported less frequently due to retaining residual diuresis. Native nephrectomy at transplantation and polycystic renal disease diagnosed before transplantation have no negative effect on graft survival. The frequency of acute rejection is comparable to that in non-ADPKD recipients [5].

An increased risk of post-transplant diabetes was observed in ADPKD recipients, and therefore education about diet and lifestyle is important in this group of patients [6]. ADPKD recipients require antihypertensive treatment that is usually initiated before transplantation, as well as prevention of cardiovascular risks. ADPKD recipients present slightly more frequently with urinary tract infections which require standard prevention/treatment. Infected native kidney or liver cysts (abscesses) pose a difficult clinical problem as they require long-term antibiotic therapy and, in some cases, surgical intervention. According to Bhutani et al. chronic rejection is the main cause of delayed graft loss in ADPKD patients (54%).

Post-transplant nephrectomy is performed in about 20% of recipients. The main indications include hemorrhage, lithiasis, infections, pain, or cancer. Notably, dimensions and volumes of native kidneys are reduced following the transplantation. Veroux et al. assessed 55 native kidneys in transplant recipients one year after transplantation to observe a 12.24–14.43% reduction in kidney size. The average total kidney volume as assessed on the MRI scan decreased significantly from 1617.94 ± 833.42 mL to 1381.42 ± 1005.73 mL ($p < 0.05$), i.e. by the average of 16.44%. The reduction in native kidney volume is probably due to the cessation of function following the transplantation [7].

The incidence of RCC in ADPKD recipients is lower than that in non-ADPKD recipients [8]. The reason for this is not clear and may be related to ADPKD's biology and less risky behaviors of ADPKD patients. As in the case of all recipients, ADPKD recipients should undergo annual abdominal ultrasound follow-up.

In the event of transplant failure and the need to initiate renal replacement treatment, consideration should be given to retransplantation — elective, pre-emptive, or after initiation of dialysis. Indications for nephrectomy should also be considered in addition to the standard qualification procedure. Usually, retransplantation is performed on the contralateral side. If there are no indications for graftectomy, the first graft should remain in place to protect the recipient from immunization; the contralateral kidney is frequently a native organ. In patients after bilateral native nephrectomy, the problem of "side" for the new graft is irrelevant, whereas in cases when one or both native kidneys are preserved, indications for nephrectomy should be assessed before transplantation [9].

SUMMARY

Survival of patients and grafts is better in ADPKD patients as compared to patients with other renal diseases. The principles of matching and immunosuppressive treatment do not differ from those in the current general guidelines. Comprehensive care for ADPKD recipients requires that potential complications typical for ADPKD be considered.

Graft function monitoring is based on evaluation of simple biochemical and histological parameters and its principles are not different from those that apply to other recipi-

ents. Pre-emptive retransplantation should be considered in progressing kidney failure. In addition to the standard qualification procedure, native nephrectomy or graftectomy may be required before retransplantation. Autotransfusion should be planned when planning the surgical procedure.

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OTHER DILEMMAS REGARDING THE QUALIFICATION OF ADPKD PATIENTS. ANEURYSMS, COLONIC DIVERTICULOSIS, AND HERNIAS

Mariusz Niemczyk, Magdalena Krajewska

Different types of anomalies in the natural history of ADPKD are the result of generalized epithelial cell differentiation defects and/or extracellular matrix dysfunction due to genetic disorders. Due to polycystin 1 being expressed in numerous tissues [1], ADPKD is a systemic disorder presenting with numerous extrarenal symptoms [2]. The most common extrarenal morphological changes include cysts within the liver and pancreas, intracranial aneurysms, cardiac valve disorders, intestinal diverticulosis, and herniations. The presence of these symptoms, as well as the risk of associated complications, must be taken into account in the process of qualifying a patient with ADPKD for organ transplantation.

Intracranial aneurysms are the most serious extrarenal symptoms of ADPKD. They occur in 10–11.5% of ADPKD patients [3, 4], i.e. about 4–5 times more frequently than in the general population [5]. The risk of an intracranial aneurysm rupture in an ADPKD patient is highest in the 5th decade of life [6], i.e. at a time when a large proportion of ADPKD patients have not yet developed end-stage renal disease and are not considered eligible for organ transplantation. Importantly, this often applies to patients with poorly controlled arterial hypertension. On the other hand, the incidence of intracranial aneurysms increases with age [7, 8] and correlates with expansion of polycystic kidneys [7], which is an indicator of the chronic renal disease progressing towards its end stage [9].

Intracerebral or subarachnoid bleeding in the course of aneurysmal rupture is a very serious potential complication. ADPKD is considered to be a risk factor for intracranial bleeding in patients undergoing dialysis treatment [10, 11] or subjected to renal transplantation [12–15]. The size of the aneurysm, its location, and the history of previous bleeding are important prognostic factors. Literature data on the prevalence of intracranial aneurysms in patients with end-stage ADPKD are limited. Kim et al. [16] demonstrated the prevalence of intracranial aneurysms in 14.9% of kidney graft recipients. Studies conducted at the Department of Immunology, Transplantation Medicine and Internal Diseases of the Medical University of Warsaw confirmed the presence of intracranial aneurysms in more than 20% of ADPKD patients who have undergone renal transplantation [17].

Routine screening in all ADPKD patients for intracranial aneurysms is not currently recommended. This is justified by the low risk of rupture of most of the observed aneurysms

[18], the relatively high cost of screening, and the potential risk of complications in the treatment of asymptomatic aneurysms [19]. Since the only recognized risk factor for the rupture of an intracranial aneurysm is positive family history [20], the *Kidney disease: Improving Global Outcomes* (KDIGO) guidelines recommend that screening for intracranial aneurysm be carried out in the following situations:

- confirmed family history;
- a patient history of intracranial aneurysm;
- 'high-risk' occupation or hobby (an airplane pilot is a typical example, but bus drivers are also at risk);
- A patient being anxious about the potential development of an intracranial aneurysm [18].
- Indications such as scheduled major surgery are also taken into account in other guidelines [21, 22] that highlight the anticoagulation and antiplatelet treatment as being a risk factor for increased bleeding upon aneurysmal rupture.

Notably, economic arguments have been increasingly raised in recent years to promote cost-effectiveness of screening for intracranial aneurysms in ADPKD patients [23, 24].

The increased incidence of intracranial aneurysms in ADPKD patients, risk of their rupture, and widespread availability of screening, as well as the current views on the economic viability of screening, make screening for intracranial aneurysms a routine element of the procedure of qualifying ADPKD patients for organ transplantation in numerous transplantation centers. For example, the Australian guidelines suggest that screening examinations be considered in all patients [21]. Such management seems appropriate and exclusion of intracranial aneurysm in the 5-year period leading to the transplant procedure should be considered in any potential recipient of an ADPKD-related transplant.

At other test centers, screening is performed in subjects with increased risk of aneurysmal rupture, i.e. family history, headaches, and/or patients requiring chronic anticoagulation therapy, albeit usually in subjects above 18 years of age (as aneurysmal ruptures are rare in the childhood period).

Screening consists of an angio-MRI scan which requires no contrast agent [18]. In patients with contraindications to MRI, angio-CT is the second-choice modality. Neurosurgical consultation is required when an intracranial aneurysm is detected. If the estimated risk of aneurysmal rupture is low, the option of watchful waiting is allowed with annual angio-MRI assessments [24] provided that modifiable risk factors are addressed (anti-hypertensive treatment, cessation of smoking, and alcohol abuse). In the case of a decision to initiate treatment, the patient is qualified for neurosurgery or endovascular procedure. The decision regarding the management is made by a neurosurgery specialist in consultation with the patient [18, 21]. If no intracranial aneurysm is detected in the first angio-MRI, the exam should be repeated after 5 years due to the possibility of later development of the lesion [24]. The risk of aneurysmal development in ADPKD patients pertains also to other arteries [25–27] but routine diagnostic screening is not recommended in these locations.

In addition to aneurysms, cardiovascular manifestations of ADPKD may also include cardiac valve defects (most commonly seen as mitral prolapse in as many as 25% of ADPKD patients), dilated ascending aorta (and associated aortic regurgitation), and thoracic aortic dissection. A trend towards familial predisposition was observed for this last complication. For these reasons, in-depth cardiac assessment is necessary in the process of qualifying ADPKD patients for organ transplantation. Echocardiography is recommended in subjects with supracardiac murmur detected in physical examination. In addition, echocardiography or cardiac MRI scan is recommended in patients with a family history of thoracic aortic dissection [28].

Polycystins — proteins encoded by the *PKD1* and *PKD2* genes – are involved in the development of the extracellular matrix [29], and therefore, colonic diverticula constitute a part of the clinical presentation of ADPKD. Colonic diverticulosis is observed in more than one-half of patients with end-stage renal disease developing in the course of ADPKD [30]. In addition, ADPKD was reported to be associated with concomitant duodenal [31] and gastric diverticula [32]. In the past, proposals were even made for preventive colon resection in patients with a history of diverticulitis to prevent another episode of diverticulitis following the renal transplant [33].

None of the current guidelines recommend screening for colonic diverticulosis in ADPKD patients qualified for kidney transplantation [18, 21, 22], and routine diagnostics in this direction is not necessary.

Abdominal wall hernias are also considered a part of the clinical presentation of ADPKD [34]. Patients treated by peritoneal dialysis are also at increased risk of developing inguinal hernias (frequently with patent processus vaginalis). As in the case of diverticulosis, routine screening for hernias in patients with ADPKD undergoing qualification for organ transplantation [18, 21, 22] is not recommended.

The possibility of Incidental detection of rare extrarenal manifestations of ADPKD, such as intracranial arachnoid cysts or peri-radicular cysts, during qualification for transplantation, is also worth mentioning [35, 36]. These are usually asymptomatic, and no treatment is required. No routine screening is also recommended in that direction. Identification of such lesions may be associated with longer times of qualification for transplantation, for example, when a peri-radicular cyst within the sacral region imitates an adnexal tumor [36]. The awareness of the possibility of incidental finding of rare extrarenal manifestations of ADPKD can save the patient from additional diagnostic examinations and reduce the time required to put the patient on the recipient waiting list [18].

SUMMARY

Due to polycystin 1 being expressed in numerous tissues, ADPKD is a systemic disorder presenting with numerous extrarenal symptoms. The most common extrarenal morphological changes include cysts within the liver and pancreas, intracranial aneurysms, cardiac valve disorders, intestinal diverticulosis, and herniations. The presence of these symptoms, as well as the risk of associated complications, must be taken into account in the process of qualifying a patient with ADPKD for organ transplantation. Particular attention should be paid to intracranial aneurysms. The risk of aneurysmal rupture and the widespread availability of screening modalities result in screening for intracranial aneurysm becoming a routine part of the organ transplantation qualification procedure for ADPKD patients at many transplantation centers.

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PERITONEAL DIALYSIS IN ADPKD PATIENTS BEFORE RENAL TRANSPLANTATION AND AFTER THE LOSS OF GRAFT FUNCTION

Monika Lichodziejewska-Niemierko, Ewa Wojtaszek

It is recommended that peritoneal dialysis be considered as the method of renal replacement treatment in patients with ADPKD both in the pre-transplantation period and after the loss of graft function

Peritoneal dialysis (PD) is a widely established method of renal replacement in ADPKD patients [1]. At numerous centers, however, it is rarely offered to these patients. In Poland, only about 4% of ADPKD patients receive peritoneal dialysis as compared to about 6–7% in Europe. At the same time, according to an Australian-New Zealand register, renal replacement therapy is started with PD in as many as 25% of patients, with no change in this percentage being observed in the years 1963–2014 [2–4].

It appears that the uncertainty regarding the possibility of qualifying ADPKD patients for peritoneal dialysis may be due to the established belief that ADPKD is a relative contraindication to PD, as well as to the low experience of dialysis teams in delivering the treatment to ADPKD patients. Results of studies from the 1980s and the early 1990s suggested that ADPKD was associated with a higher risk of mechanical complications due to high intraabdominal pressure (hernias, dialysate leaks), infectious complications (due to urinary tract/cysts infections or diverticulosis) and problems with obtaining adequate dialysis due to reduced peritoneal space resulting from enlargement of kidneys and liver.

However, single- and multi-center studies, as well as meta-analyses carried out in recent years, show that PD is an effective and safe method of renal replacement therapy. Its advantages consist in the longer maintenance of residual renal function, the patient's ability to continue with normal social and professional activities, good quality of life, and safety during the pandemic period. In addition, peritoneal dialysis seems to be a good choice as a bridging therapy before kidney transplantation. In Spain, the '*PD first*' model was shown to function well in combination with an active transplantation program in ADPKD patients, and it shortened the time to transplantation compared to hemodialyzed patients [5, 6].

Peritoneal dialysis is also a good choice in patients with ADPKD returning to dialysis therapy due to failure of the transplanted kidney. Persistent diuresis constitutes an advantage and makes it easier to control the hydration status with liberal liquid intake. The presence of the graft and the continuation of treatment with reduced doses of steroids and calcineurin do not increase the incidence of complications, including infective complications, compared to non-ADPKD patients. Patients in whom quick retransplantation, particularly a living organ retransplantation, is planned, may benefit from PD due to better performance early in the period following the loss of the graft function [7].

Studies and meta-analyses published in recent years suggest that the results of PD in ADPKD patients are at least comparable to those of PD in patients with renal failure of different etiology or those of hemodialyzed (HD) ADPKD patients.

In a systematic review of 12 studies comparing the results of PD in ADPKD and non-ADPKD patients, Zhang et al. observed no differences in the adequacy and frequency of dialysis complications and failure or total mortality rates and individual causes of death. At the same time, the percentage of renal retransplantation was significantly higher in ADPKD patients [8]. The authors also demonstrated similar survival for ADPKD patients receiving PD vs HD [8]. Similar results were obtained by Sigogne et al. in a retrospective analysis of data from French registers. Based on the REIN (*Renal Epidemiology and Information Network*) data, the 5-year survival of patients with ADPKD treated with PD and HD was found to be the same, with age and diabetes being the only risk factors of death as identified in multi-factor analysis. A significantly higher number of PD-treated patients received renal transplants in the study period [9]. In turn, the data within the RDPLF (*Registre de Dialyse Péritonéale de Langue Française*) register were used to compare the outcomes for PD-treated patients with ADPKD and other etiologies of renal failure. The same values of prevalence and time to the first episode of peritonitis and the same time-to-method-failure values were observed in ADPKD and non-ADPKD patients. However, the frequency of renal transplantation and graft survival were significantly better in ADPKD patients, albeit the group was characterized by significantly younger age and lower comorbidity rates than the group of non-ADPKD patients. Similarly, in a meta-analysis carried out by Dupont et al., the survival of patients with ADPKD was better than that of the remaining subjects, which may have been due to younger age, lower comorbidity rate, and hemoglobin levels [10]. On the other hand, it is stressed that survival may be improved by early diagnosis of genetic disease, good patient management during the pre-dialysis period, optimum treatment initiation time, and optimized individualized decisions regarding the renal replacement therapy method to be undertaken.

Some studies have seen a higher incidence of complications due to high intraabdominal pressure — hernias and leaks into the pleural cavity — in patients with ADPKD. However, no need to permanently discontinue PD was observed for any of these complications [4, 10, 11]. Time to method failure was similar to that in non-ADPKD patients, and no correlation was confirmed between renal size and method failure [12]. Renal transplantation eligibility rates were comparable in both groups of patients [10].

The mode of peritoneal dialysis and the treatment of complications in ADPKD patients are similar to those in patients with other etiologies of chronic kidney disease.

Both continuous ambulatory peritoneal dialysis (CAPD) and automated peritoneal dialysis (APD) can be used in ADPKD patients. The choice of method is generally determined by the patient to achieve their life goals and priorities while maintaining acceptable quality of life [13]. The size of the kidney and the presence of hernias may constitute an indication for APD with lower peritoneal filling volumes at night.

Some studies suggested that abdominal hernia and dialysate leaks are more common in ADPKD patients as compared to non-ADPKD patients [4, 10, 14]. The relationship might have been due to the CAPD mode with a total volume of 2 liters of dialysis fluid being used in earlier years. Hamauoue et al. observed that the incidence of these complications was higher in patients with giant kidney and liver sizes [15]. On the other hand, Signone et al. showed that only a high body mass index, rather than the volume of kidneys and liver, is a risk factor for increased intraabdominal pressure and mechanical complications of dialysis associated therewith [16].

Abdominal complications, such as hernias, were also found to be more frequent in patients with ADPKD at all stages of chronic kidney disease. Therefore, it is likely that hernias may be directly associated with collagen defects rather than with increased intraabdominal pressure and may be observed in ADPKD patients receiving other types of renal replacement therapy [17].

The risk of mechanical complications seems to be reduced in patients with organomegaly treated with APD. During the procedure, the patient remains in a horizontal position and lower filling volumes can be used for nocturnal cycles; the last filling can remain within the peritoneal cavity during the day.

Hernia is not an absolute contraindication for an ADPKD patient to be qualified for PD. However, it seems reasonable to perform hernia repair using a Prolene mesh before or simultaneously with Tenckhoff catheterization. Diagnosis and treatment of hernias and dialysate leaks during PD are the same as those used for non-ADPKD patients.

Consideration should be given to the decision and timing of nephrectomy that is performed as part of preparing the patient receiving peritoneal dialysis for renal transplantation, as well as in a patient undergoing peritoneal dialysis following the loss of graft function.

The maintenance of residual renal function and diuresis improves survival of dialyzed patients; during PD treatment, it also contributes to optimizing treatment at moderate doses of dialysis fluids. A more controlled balance of liquids and electrolytes can have a beneficial effect on cardiovascular morbidity, nutrition status, and quality of life [18]. Following native nephrectomy, a significant drop is observed in renal clearance and diuresis which are reduced by as much as one-half, requiring an increase in doses and glucose concentrations of dialysis fluids to achieve satisfactory particle clearance and ultrafiltration.

Preventive nephrectomy should, therefore, be performed only in ADPKD patients who suffer from recurrent severe infections or intracystic bleedings and before transplantation in cases of organomegaly and the need to make room for the transplanted kidney. To reduce the number of serious interventions and eliminate the need for a temporary interruption in PD, some centers offer to perform nephrectomy procedures simultaneously with renal transplantations [19, 20]. Such a possibility is worth considering, particularly if the patient continues to receive DP with good adequacy of treatment, good quality of life, and no complications. Indications for nephrectomy have been discussed in detail earlier in this article.

In patients returning to DP, nephrectomy of the allograft is not necessary if the graft failure is asymptomatic. Indications for graftectomy are the same as in patients returning to HD treatment [7]. If the loss of graft function was due to nephropathy associated with BK virus (BKV) infection and/or high viremia persists, graftectomy may be considered before PD initiation, with the possibility of a peritoneal catheter being implanted as part of the same procedure. However, nephropathy due to a BKV infection is not an absolute indication for the removal of the failed kidney before qualifying the patient for retransplantation. Graftectomy will be required in about one-third of all patients with late loss of graft function [21].

Effective nephrectomy facilitates optimum preparation of the patient for the transplantation procedure [21]. The recommended surgical procedure involves the sparing of the peritoneal membrane and cavity with extra-

peritoneal access preferred for nephrectomy procedures. Laparoscopic-assisted retroperitoneal nephrectomy (LARN) can be used for this purpose [22]. An HD catheter should be implanted before or during the nephrectomy procedure as temporary HD is required in most cases due to the disrupted peritoneal continuity. In an observational study by Ietto et al., the mean duration of temporary hemodialysis was 35 days [23]. In cases of graftectomies, it is recommended that discontinuation of PD lasts approximately 4 weeks. Due to the possibility of hernias developing in post-nephrectomy scars, APD (*ambulatory peritoneal dialysis*) should be considered, particularly in the early period after the surgery [24]. Usually, reduction or elimination of diuresis necessitates an increase in the dose and composition of dialysis fluids.

SUMMARY

The KDIGO recommendations point to PD as an alternative to HD before renal transplantation and after graft function loss [25, 26]. Safety, comparable or better survival and good quality of life associated with the method make PD suitable for as either temporary (prior to transplantation) or as target renal replacement therapy.

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