

Polycystic renal disease

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Abstract

Polycystic kidney disease (PKD) is a leading cause of end-stage renal disease (ESRD). Urinary tract infections (UTI) occur in 21–75% of patients with autosomal dominant polycystic kidney disease (ADPKD) and as high as 50% have been reported in patients with autosomal recessive polycystic kidney disease (ARPKD) during their lifetime. Frequently UTI is the first presentation of the disease. The urinary tract, renal parenchyma and cysts may be involved in the inflammatory process. Renal infection is a common occurrence in ADPKD and often leads to serious complications, including infected cysts, perinephric abscess, septicemia, and death. Important predisposing factors include age, female sex, and recent instrumentation of the urinary tract and diabetes mellitus. Gram-negative enteric organisms most commonly cause renal infections in PKD. Diagnosis of these infections may be difficult since some patients do not have bacteriuria. CT or MRI (or both) may be helpful in some patients with UTI and is often superior to sonography for detecting cysts in organs other than the kidney. In recent years, 18FDG-PET/CT has shown to be the most sensitive and accurate modality for diagnosis of infected cysts. Eradication of cyst infections with conventional antibiotic therapy can be difficult despite proven in vitro sensitivity of the causative organisms to the agents administered and in some cases, percutaneous drainage is indicated.

Keywords: Autosomal dominant polycystic kidney disease (ADPKD), autosomal recessive polycystic kidney disease (ARPKD), urinary tract infection (UTI), polycystic renal disease, pyelonephritis, cyst infections, diagnostics and treatment PKD

Summary of recommendations

1. Uncomplicated lower urinary tract infection (UTI), cystitis, urethritis, in patients with autosomal dominant polycystic kidney disease (ADPKD) should be managed according to the same principles as in patients with normal urinary tracts (GoR B).
2. Renal infections of patients with ADPKD should be subclassified as pyonephrosis (infection of the upper collecting system), acute bacterial interstitial infection (infection of the renal parenchyma) or pyocyst (infection confined to a cyst) (GoR B).
3. Diagnostics of pyocysts can be most challenging and, if effective treatment is delayed, severe infections with risk of systemic spread may occur. Therefore, serial blood and urine cultures are essential before starting antibiotic therapy (GoR B).
4. For the majority of infections in patients with ADPKD and autosomal recessive polycystic kidney disease (ARPKD) common uropathogenic *Enterobacteriaceae* have to be considered, e.g.: *E. coli*, *Klebsiella*, *Proteus*, and *Pseudomonas spp.* (GoR B).
5. Computer Tomography (CT) imaging, perhaps supplemented with magnetic resonance imaging (MRI) (if renal function is normal), is optimal in the evaluation of a febrile patient with ADPKD, to detect infected cysts, pyonephrosis and perinephric abscess (GoR B). Positron Emission Tomography (PET) using 18-Fluorodeoxyglucose (18FDG) has shown some promising role for the accurate diagnosis and localization of suspected infected renal cysts (GoR B).
6. Lipid-soluble antibiotics should be selected for the treatment of infected renal cysts. Of these, fluoroquinolones are the most effective and should be prescribed empirically if suitable according to the local susceptibility pattern (GoR B).
7. Nephrectomy is still occasionally necessary to prevent recurrent UTI and its complications, particularly if transplantation is imminent and the infecting organisms are resistant (GoR B).
8. Nephrectomy may also be recommended if removal of infective stones is impossible by conservative surgery or percutaneous nephrolithotomy.
9. Tolvaptan-vasopressin V2 receptor antagonist showed beneficial effect on delaying the progression of ADPKD, however the routine use of tolvaptan is not recommended, without additional evidence from large clinical trials (GoR B).

1 Introduction

Polycystic kidney disease (PKD) is a leading cause of end-stage renal disease (ESRD) [1], [2]. Renal insufficiency, severe pain due to hemorrhagic expansion of the cysts, or infections are the most common clinical presentations [3]. The estimated incidence of infections of renal cysts in patients with autosomal dominant polycystic kidney disease (ADPKD) is 1 episode per 100 patients per year [4], [5]. In patients with autosomal recessive polycystic kidney disease (ARPKD) urinary tract infections (UTI) occur in 50%, with greater frequency in girls than in boys [6]. If UTI is diagnosed in a child, vesico-ureteral reflux, obstruction, or bladder dysfunction should be ruled out [5], [7]. Known predisposing factors include advanced age, female gender, diabetes mellitus and instrumentation of the urinary tract as the presumed mode of infection is retrograde migration of bacteria through the ureters, while hematogenous seeding is less likely [8]. Often both kidneys are involved in the infectious process. Isolated cyst infections (negative urine culture and absence of white blood cell casts in urinary sediment) are more frequent, than acute or chronic pyelonephritis (urinary sediment positive for white blood cell casts) [9].

Frequently UTI is the first and leading presentation of the disease. It occurs more often in women due to the ascending infection of lower urinary tract (urethritis, cystitis), similarly to patients without ADPKD [10], [11], [12] (GoR B, LoE 3). Asymptomatic bacteriuria is not more frequent in ADPKD patients with normal kidney function and without diabetes mellitus than in healthy people [13].

The more severe clinical manifestations of upper tract UTI are common and tend to occur after instrumental intervention and bladder catheterization when there is an increased risk of colonization by nosocomially acquired polyresistant bacterial strains [14], [15], [16] (GoR C, LoE4). Percutaneous nephrolithotomy (PNL) in patients with ADPKD can have more postoperative complications such as bleeding requiring transfusions, and fever due to cyst infection [17]. Unilateral nephrectomy is a well-founded surgical treatment before kidney transplantation. There are contradictory data on the feasibility of bilateral nephrectomy in patients with ADPKD before or during kidney transplantation [18]. Bilateral nephrectomy before or during transplantation eliminates ADPKD complications and does not significantly increase general complications. The patients could benefit from reduction of the operative procedures, better relief from persistent arterial hypertension and lower UTI posttransplantation. The highest numbers of complications and of graft losses were observed among the group without pretransplantation nephrectomy [19], [20], [21], [22].

In recent years, 18-Fluorodeoxyglucose (18FDG)-Positron Emission Tomography (PET)/Computer Tomography (CT) has shown to be the most sensitive and accurate modality for the diagnosis of infected cysts. Recently, Tolvaptan, a selective arginine vasopressin V2 receptor antagonist, showed good results in reduction of cysts and reduce the speed of disease progression in selected patients [23].

2 Methods

A systematic literature search was performed in PubMed, Medline, the Cochrane data base and in books, journal articles (in English and Russian) with the following key words: “autosomal dominant polycystic kidney disease (ADPKD)”, “autosomal recessive polycystic kidney disease (ARPKD)”, “urinary tract infection (UTI)”, “polycystic renal disease”, “pyelonephritis”, “cyst infections”, “treatment ADPKD” without limitation on gender, age, clinical studies. In the first edition [24], searching the literature from 1985 to 2009, a total of 368 English publications and three Russian monographs were identified and reviewed after screening by title and abstract. Now, only literature published after 2009 was reviewed.

In this article only literature published after 2009 was reviewed and 366 publications were found. After screening by title and abstract and exclusion of duplicates a total of 95 were included into the analysis. The studies were rated according to the level of evidence and the strength of recommendations according to the ICUD standards (see preface) [25], [26].

3 Clinical manifestation

The urinary tract should always be suspected as the most likely source of infection in the febrile patient with PKD [27]. The urinary tract per se, renal parenchyma and cysts may be involved in the inflammatory process. UTI associated with ADPKD can occur secondarily in association with a variety of urological problems which are themselves more common in ADPKD and can predispose to infection e.g. nephrolithiasis, recurrent gross haematuria requiring repeated endoscopy, and obstruction of renal outflow (extrinsically by cysts, intraluminally by blood clot and debris) [17].

Renal infections can be subclassified as pyonephrosis (infection of the obstructed upper collecting system), acute bacterial interstitial infection (infection of the renal parenchyma), or pyocyst (infection confined to a cyst) [5]. Pyocysts are potentially the most serious of the three as diagnosis may be difficult and delayed. Failure of a short course antibiotic therapy given empirically to a febrile patient with nonspecific symptoms may be indicative for pyocysts [28] (GoR B, LoE 2b). Pyocysts are in most instances accompanied by previously unreported loin pain and tenderness, and positive blood cultures. Usually Gram-negative enteric organisms are responsible, which suggests an ascending route of infection. Efficacy of antibiotic treatment and infection eradication are defined by disappearance of fever, normalization of CRP levels, and at least two negative blood and/or urine cultures.

Displacement of renal parenchyma with cysts eventually leads to chronic renal insufficiency. UTI may play a role in the decline of renal function but the evidence is surprisingly equivocal [29] (GoR C, LoE 4).

The incidence of kidney calculus in ADPKD patients ranges from 8% to 36% [30], [31], [32], thus much higher than in general population, while ADPKD with staghorn calculi is rare. In general population, staghorn calculi were traditionally believed to be synonymous with infection stones, and secondary to UTI. However, recent data challenged this traditional opinion. In a retrospective analysis with 52 kidneys with complete staghorn calculi, 56% of the kidney stones were metabolic and 44% were infection stones [33].

UTI is very common in ADPKD with 30%–50% patients experiencing an episode of UTI in their lifetime [11], [34], [35]. Thus UTI is an important complication for PKD patients and will facilitate the formation of staghorn calculi. As staghorn calculi are associated with kidney fibrosis and a high rate of long-term renal deterioration, prompt control of UTI in ADPKD patients will be beneficial in preventing staghorn calculus formation [3].

4 Diagnosis

4.1 Clinical symptoms and laboratory evaluation

The diagnosis of cystic infections is usually based on clinical grounds when patients develop systemic symptoms such as fever, weight loss and malaise often in combination with abdominal or back pain [38], [39]. The diagnosis can be quite straightforward, when symptoms are combined with elevation of laboratory markers of inflammation such as erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), procalcitonin test and fibrinogen, but there are no established cut off values for these parameters [40]. On the other hand, to prove that a patient is indeed affected by infection of a renal cyst is quite difficult, as the gold standard requires the analysis of the content of the responsible cyst. This is often not feasible nor recommended especially when there is no clear identification which cyst is infected.

Usual radiologic examinations are often of little help in the diagnosis of cyst infections [41]. For instance, ultrasonography, CT, and magnetic resonance imaging (MRI) failed to detect the infected cyst in 94%, 82% and 60% of cases, respectively, and most importantly yielded negative results in more than half of patients with a definite diagnosis of cyst infections [5], [42]. In contrast, PET scan proved highly efficient in identifying renal and hepatic infected cysts in all tested patients (GoR B, LoE 2b) [43], [44]. These data [5] confirm recent reports underlining the high performance of PET scan in the diagnosis of cyst infections. PET scan is a reliable tool for the detection of tissue infection, on the basis of the high metabolic activity and increased uptake of the glucose analogue FDG in inflammatory cells [45], [46].

Diagnosis of a simple UTI is made as usual on the basis of positive urine culture in combination with one or more clinical symptoms – dysuria, back pain with typical radiation, pyrexia and even rigors. Pyuria, leukocytosis, and bacteraemia are usually present [28] (GoR B, LoE 2b). Positive urine culture and pyuria favour renal parenchymal infection but a positive blood culture with discrete abdominal or flank tenderness, sometimes with a negative urine culture is consistent with infection in a cyst. PET scan is probably the first-line optimal tool for the detection of infected cysts in patients with ADPKD and patient follow-up after antibiotic therapy. It may also prove helpful for defining new diagnostic criteria for cyst infections in patients with ADPKD; however, to the best of our knowledge, PET scan has not been evaluated in intracystic bleeding, the main differential diagnosis of cyst infections in patients with ADPKD. Moreover, increased FDG uptake has been reported in the setting of hematoma occurring in various extrarenal sites. Thus, the specificity of PET scan for cyst infections remains to be assessed. Thus, significant intracystic bleeding usually had been ruled out by CT scan in patients who had ADPKD and were undergoing a PET scan for suspected cyst infection.

Renal infection has been reported in 12% to up to 26% of patients with ADPKD undergoing hemodialysis and predialysis history of cyst infections correlates with the occurrence of similar infectious events on hemodialysis [47].

The majority of infections are caused by uropathogenic Enterobacteriaceae. Common pathogens include *Escherichia coli* (74% of positive cultures) and other enteric flora and cyst infections accounts for 10–15% of all causes of hospitalizations of ADPKD patients [5]. Microorganisms isolated from renal cysts usually include Gram-negative uropathogenic bacteria with *E. coli* accounting for three quarters of cases (GoR A, LoE 1a). This finding suggests an ascending mechanism for cyst infection, at least in the case of positive urine culture. *Streptococcus*, anaerobic gas-forming bacteria, and *Candida albicans* have been previously reported in infected cysts in patients with ADPKD as well [48], [49], [50], [51], [52]. The low oxygen tension within cysts may support the potential for anaerobic infections. Repeated antibiotic courses and drainage and surgery procedures may also lead to the emergence of nosocomial bacterial strains.

Such infections can have serious consequences and patients who are waiting for a renal transplant should be put on hold until their infection is resolved since bacteraemia and sepsis can result in graft loss or perioperative death [53]. Similarly, patients who are immunosuppressed after renal transplantation can develop serious infections in the native polycystic kidneys cysts that can be responsible for systemic complications due to their attenuated immune response.

Jouret et al. [53] have proposed clinical criteria for the diagnosis of infected cysts in patients with ADPKD. These criteria are:

1. presence of neutrophils and bacteria in the fluid aspirate from the suspected cyst; or alternatively,
2. the concurrent manifestation of fever (temperature $>38^{\circ}\text{C}$ for >3 days), abdominal tenderness in the area of the polycystic kidney, increased serum CRP levels (>5 mg/dL) and the absence of CT findings suggestive for recent intracystic bleeding (intracystic density <25 Hounsfield units) [5].

Although these criteria are important to initiate and direct the duration of systemic antibiotic therapy, they are not helpful for the identification of which cysts are infected [54].

In addition, the diagnostic accuracy of these tests is further limited by the fact that contrast agents cannot be used in the presence of renal dysfunction in patients with ADPKD [55], [56]. Recently, there has been some enthusiasm around the use of scintigraphy with indium- or gallium-labelled leukocytes as some investigators have reported promising results in localizing infected cysts [57]. However, one of the limitations of this technique is the fact that it is not universally available, it is quite costly and provides a relatively poor spatial discrimination when patients have severe anatomical distortion of their native kidneys [58], [59].

Cysts can become secondarily infected by the haematogenous route. *Staphylococcus aureus* infection established by cyst fluid and blood cultures has been reported in an intravenous drug abuser and in a peritoneal dialysis patient after staphylococcal peritonitis [60], [61] (GoR B, LoE 2a).

4.2 Imaging

X-rays and tomograms may reveal evidence of peri-renal infection and nephrolithiasis. Sonography is commonly used as a preliminary form of imaging but it can be very difficult to identify the development of an abscess within a complex septate cyst containing echodense proteinaceous deposits suspended in serosanguinous cystic fluid. Multislice CT is regarded as mandatory to make the diagnosis and plan further treatment, though MRI may ultimately prove as effective without risk of radiation exposure [62] (GoR B, LoE 3). In the past, 67 Gallium isotope scintigraphy was used to detect areas of inflammation [63], [64]. The value was limited by excretion of a significant fraction of the dose into the bowel. Furthermore it was reliable in detecting only 50% of infected cysts, though in one study it was helpful in identifying the focus of persistent UTI in renal transplant recipients with underlying ADPKD. Sensitivity may be improved with gallium SPECT [57]. Indium labeled leucocytes may have offered advantages as a carrier but these techniques are rarely used except in the research environment [65] (GoR C, LoE 3).

PET using 18FDG has shown some promising role for the accurate diagnosis and localization of suspected infected renal cysts. One of the advantages of 18FDG is that it is not nephrotoxic and can be successfully used in patients with ESKD [53], [66]. In addition, when associated with CT scanning, 18FDG-PET/CT has good spatial discrimination, which may allow the guiding of percutaneous procedures or the study of the adjacent tissues. Soussan et al. [67] evaluated the diagnostic criteria in renal and hepatic cyst infection and found that 18FDG-PET/CT identified 100% of definitive and 93% of probable cyst infection cases [67]. Another group [68] also reported that 18FDG-PET/CT yielded positive results in 87% of cases of infected cysts. Jouret et al. [69] reported that in their experience 18FDG-PET was able to identify distinct non-cystic infectious conditions such as ischemic colitis, diverticulitis, retroperitoneal abscesses, prostatitis, pyelonephritis, and infected abdominal aorta aneurysm and that 18FDG-PET changed the management of 26% of patients who were initially diagnosed with suspected infected renal cysts. In fact, the diagnostic performance of 18FDG-PET has not been fully evaluated for intracystic bleeding that is the main differential diagnosis of cyst infection in ADPKD patients and accumulation of 18FDG has been described in the setting of hematomas outside the renal parenchyma [70]. Therefore, the specificity of 18FDG-PET/CT for renal cyst infections remains unknown at this point [71]. However, despite the fact that 18FDG-PET/CT is a promising tool for the diagnosis and follow-up of infected renal cysts, the low availability and its high costs that are similar to scintigraphy with labeled white blood cells will limit its wider use.

5 Treatment

The main treatment for suspected infected renal cysts is systemic antibiotic therapy for 3 to 6 weeks [5]. The selection of the type of antibiotic is usually empirical as the results of blood and urine cultures lag behind the clinical presentation [72]. Despite this limitation, in a large cohort of patients treated in the United Kingdom, the clinical efficacy of the initial antibiotic therapy was observed in 71% of infections [5].

The majority of patients respond to antibiotic therapy without the need for any other intervention. However, for a small group, percutaneous drainage of suspected large (>5 cm) infected cysts may be beneficial as antibiotics often do not have the ability to reach the concentration necessary to sterilize the cystic fluid.

The efficacy of antibiotic treatment may depend on the liposolubility of the agents used and whether or not they are ionized at physiological pH. Intracystic pH determines the extent to which basic lipophilic antibiotics accumulate in the fluid. Lipid-soluble antibiotics which are relatively alkaline may be useful in the treatment of infected renal cysts [73], [74] (GoR A, LoE 2b).

Betalactam and aminoglycoside broad spectrum antibiotics are often ineffective for treatment of cyst infections, possibly because these antibiotics require active transport [5], [75]. Fluoroquinolones are generally the most effective, as they have high lipid solubility and accumulate in gradient cysts [5] (GoR A, LoE 3). Cyst infection is assumed to be present by default in patients with suspected acute pyelonephritis who do not respond to standard antibiotic regimes. However, increasing rates of resistance against fluoroquinolones because often used non-selectively and the wide distribution of extended spectrum beta-lactamases (ESBLs) in major pathogens of UTI limit the choice of antibiotics [54], [76]. In selected patients with good renal function or on haemodialysis, aminoglycosides can be used as monotherapy or in combination with other antibiotics when other antibiotics fail.

Much of the details on antibiotic transport has been derived from studies on uninfected cysts. Very little is known however, how an infection effects the epithelial function and thus the antibiotic transport. After initial efficacy has been confirmed, a prolonged course (four to eight weeks) of the antibiotic therapy may be required to sterilise a pyocyst [28]. Percutaneous drainage of antibiotic-unresponsive pyocysts may be required to obtain material for diagnosis and culture adapted antibiotic therapy [77] (GoR B, LoE 3).

A pilot study was performed on adult PKD patients to examine the effects of the anti-proliferative mammalian target of rapamycin inhibitor sirolimus on the growth of renal cysts. Eight consecutive PKD patients were given sirolimus (1 mg/d PO) for 6 consecutive months, in addition to an angiotensin receptor blocker (ARB), namely telmisartan. Another 8 PKD patients served as a control group given only telmisartan [78], [79]. Hematologic tests were normal in all patients. There was an insignificant rise in kidney volume as measured by MRI in the sirolimus group (2,845 vs. 3,221 mL after 6 months; P=NS) compared with a significant increase in the control group (2,667 v.s 3,590 mL after 6 months; P< .05). The authors concluded that sirolimus, in addition to an ARB, might be beneficial for PKD patients who present early in their illness. Treatment of ADPKD patients with sirolimus with a dose of 1–2 mg/day is safe and does not cause proteinuria or impairment the level of glomerular filtration [79].

6 New treatments

Tolvaptan is the first pharmaceutical agent approved to slow the progression of cyst development and renal insufficiency of ADPKD [80]. Tolvaptan-vasopressin V2 receptor antagonist is orally active, has a half-life of about 12 hours and it is approved for the treatment of hyponatremia [81].

In the TEMPO 3:4 trial, which tested the efficacy of the vasopressin V2 receptor antagonist tolvaptan [82], 1,445 patients with ADPKD were randomized to receive either placebo or tolvaptan in a split-dose regimen of 45 mg in the morning and 15 mg in the afternoon, uptitrated to 90/30 mg when tolerated. The intention-to-treat analysis of this study showed that tolvaptan slowed the rate of total kidney volume (TKV) growth by 49% from 5.5 to 2.8% per year, and the rate of estimated GFR (eGFR) loss on treatment by 26% from 3.70 to 2.72 ml/min/1.73m² per year during the median observation period of 3 years. The renoprotective efficacy of tolvaptan in ADPKD compares well with the 15% reduction in eGFR decline (5.2 vs. 4.4 ml/min/1.73m² per year) and 15% reduction in creatinine clearance decline (6.5 vs. 5.5 ml/min/1.73m² per year) in the RENAAL and IDNT trials, respectively, which tested angiotensin-2 receptor antagonists in patients with type 2 diabetes and kidney disease.

Based on the results of the TEMPO 3:4 trial, the EMA approved in May 2015 the use of tolvaptan for ADPKD [83]. Tolvaptan has received approval for the treatment of ADPKD now in Canada, Great Britain, Europe and Japan [81]. Patients taking tolvaptan must drink volumes of water reaching 4 to 5 liters per day; consequently, its use is associated with aquaretic side effects (polyuria, nocturia, and rarely, hypernatremia). Hepatotoxicity, manifested by elevated liver enzymes has been observed, but is reversible upon withdrawal of the drug. Elevated plasma uric acid concentrations and gout may also be encountered. Therefore, the benefits of tolvaptan must be carefully weighed against the associated risks for each individual patient.

Recent evidence has highlighted the beneficial effect of tolvaptan on delaying the progression of ADPKD. The TEMPO 2:4 trial examined long-term (3 years) safety, tolerability and efficacy of tolvaptan in a multicenter open-label study [82], [84]. Overall 96% of patients taking a daily dose of 60 mg tolerated the treatment well and had an annual total kidney volume change of 1.7%+3.5% compared to 5.8%+4.3% for the control group ($p < 0.01$). These findings were confirmed by a subsequent randomized phase III multicenter double blind placebo controlled trial TEMPO 3:4 [85]. The benefits of tolvaptan appeared enhanced in patients older than 35 years, with hypertension or total kidney volume of 1,500 ml or higher at baseline. Limited data of the effect of tolvaptan are available for patients with more advanced ADPKD. Expert opinion and the results of these randomized studies indicate that any intervention in later stages of ADPKD is likely to be futile in slowing the progression of the disease and therefore the routine use of tolvaptan is not recommended without the additional evidence from large clinical trials (GoR A, LoE 1b).

7 Nephrectomy

Nowadays, nephrectomy is rarely required in the context of infection prevention but unilateral nephrectomy is a well-founded preliminary surgical treatment before kidney transplantation [19]. However, bilateral nephrectomy is still essential in patients whose confirmed suppurative pyocysts have not been sterilised before renal transplantation and immunosuppressive medication is administered. The patients could benefit from reduction of the operative procedures, better relief from arterial hypertension persistence and lower urinary tract infection posttransplantation [20]. The risk of recurrent severe UTI and cyst infection occurring after transplantation is considerable in patients with a history of pre-transplant infection [28], [86] (GoR B, LoE 3). Other indications include antibiotic resistant infection in association with renal stones where clearance cannot be achieved by standard minimal invasive techniques; accelerated drug resistant hypertension; acquired renal cystic disease with risk of malignancy and very rarely, persistent heavy haematuria. The greatest numbers of complications and of graft losses were observed among the group without pretransplantation nephrectomy [21], [22].

Minimal operative differences were seen between unilateral or bilateral two-stage nephrectomy or bilateral simultaneous open or retroperitoneal laparoscopic nephrectomy. The optimal timing is still debatable [87], [88] (GoR B, LoE 3).

Patients with ESRD due to ADPKD are effectively treated by long term dialysis and renal transplantation, with graft and patient survival scores similar to that of the general renal transplant population [89], [90] (GoR B, LoE 2a).

8 Extrarenal infection and ADPKD

Hepatic cysts occur in 58–83% patients with ADPKD [91], [92]. They are more prevalent and tend to be larger in women and in the elderly of both sexes [91] (GoR B, LoE 2a). Cysts are isolated from the biliary excretion system and therefore rarely infected; however, suppuration with multiple abscess development is still possible, particularly in renal graft recipients [93], [94]. If so, bacteraemia is common and unlike non-cystic pyogenic liver abscesses, a single bacterial species is usually responsible, suggesting a haematogenous origin for the infection. In accordance with previous reports drainage and antibiotics in combination prove more efficacious than antibiotics alone in hepatic cyst infections [5], [94]. The most serious complications of hepatic cyst are bacterial cholangitis and bleeding varices. ARPKD patients with extensive dilatations of intrahepatic and extrahepatic bile ducts are at increased risk of ascending bacterial cholangitis. Development of fever or rarely a sudden elevation of liver function tests at any time should raise the suspicion of cholangitis and appropriate evaluation and antimicrobial therapy should be initiated. From the time of initial diagnosis, all patients with ARPKD should be evaluated by a gastroenterologist and undergo regular evaluations for hepatobiliary complications. Recommended evaluation should include periodic imaging by either magnetic resonance cholangiopancreatography (MRCP), MRI or ultrasound on an annual basis for increased liver echogenicity, hepatobiliary abnormalities and splenomegaly [94].

9 Further research

The excellent sensitivity of 18FDG-PET and the spatial discrimination obtained by combining 18FDG-PET with CT reported by Lantinga et al. [68] and more recently by Jouret et al. [69] should be explored further by other well-designed studies to determine the exact diagnostic sensitivity and specificity of 18FDG-PET/CT across a wide spectrum of disease presentations.

10 Conclusion and perspective

Approximately 40–50% of patients affected by PKD are symptomatic and clinicians should be familiar with all the possible modalities that are currently available to care for these challenging patients. Selective antagonist arginine vasopressin V2 receptor, has been shown to reduce the speed of disease progression in selected patients. Cyst infections in patients with ADPKD remain a challenging diagnostic and therapeutic issue. PET scan will probably make the diagnosis of cyst infections easier and more accurate. 18FDG-PET/CT has shown to be the most sensitive and accurate imaging modality for diagnosis of infected cysts. The majority of these infections respond to systemic antibiotic therapy, but in some cases, percutaneous drainage is necessary. The identification of the infectious agent by blood and urine cultures is essential in tailoring the type and duration of the antibiotic therapy. Nephrectomy of native polycystic kidneys is necessary when patients are symptomatic and fail other modalities. Surgical therapy is also indicated to remove the large volume of a native kidney that occupies the iliac fossa of patients in need of renal transplantation. PET scan will probably make the diagnosis of cyst infections easier and more accurate. Antibiotic combination, including a fluoroquinolone, remains the main medical treatment for cyst infections. Large (diameter >5 cm) infected cysts, particularly liver cysts, require drainage in combination with antibiotic treatment.

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Citation note: Perepanova T, Apolikhin O. Polycystic renal disease. Version: 2018-03-01. In: Bjerklund Johansen TE, Wagenlehner FME, Matsumoto T, Cho YH, Krieger JN, Shoskes D, Naber KG, editors. *Urogenital Infections and Inflammations*. Duesseldorf: GMS; 2017-. DOI: 10.5680/luhui000005

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