Renal Disease and Transplantation Forum
2022, vol. 15, no. 2, 95–109

ISSN 2720–2771
e-ISSN: 2720-4189
DOI: 10.5603/RDTF.2022.0008

Alicja Dębska-Ślizień[1], Roman Danielewicz[2], Magdalena Jankowska[1], Hanna Suchanek[3], Maciej Kosieradzki[2], Marcin Matuszewski[4]

[1]Department of Nephrology, Transplantology and Internal Medicine, Medical Faculty, Medical University of Gdańsk
[2]Department of General and Transplant Surgery, Medical Faculty, Medical University of Warsaw, University Clinical Center of the Medical University of Warsaw
[3]Department of Internal Medicine, Connective Tissue Disease and Geriatrics, University Clinical Center in Gdańsk
[4]Department of Urology, Medical Faculty, Medical University of Gdańsk

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

ABSTRACT

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

Renal Disease and Transplantation Forum 2022, vol. 15, no. 2, 95–109

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

INTRODUCTION

Alicja Dębska-Ślizień, Roman Danielewicz

The principles of care for patients with autosomal dominant polycystic kidney disease (ADPKD), are in another document developed by the ADPKD Working Group of the Polish Nephrology Society (PNS, pol. *Polskie Towarzystwo Nefrologiczne*, PTN). They have already published a guide for patients (*Autosomalna dominująca wielotorbielowatość nerek: poradnik dla pacjentów oraz ich rodzin*, Gdańsk 2017), a position statement on molecular diagnosis and genetic counseling in ADPKD. *Diagnostyka molekularna i poradnictwo genetyczne w ADPKD*, 2018, as well as *Zasady postępowania z chorymi na autosomalnie dominujące wielotorbielowate zwyrodnienie nerek (ADPKD) i inne torbielowate choroby nerek*, 2019.

Autosomal dominant polycystic kidney disease is the most common genetic kidney disorder with an incidence ranging from 1:1000 to 1:400 in the general population. Approximately 70% of patients develop chronic renal failure at the average age of 58, which makes ADPKD the fourth most common indication of renal replacement therapy in the world. In Poland, ADPKD patients constitute 8% of patients starting renal replacement therapy each year. The preferred form is a kidney transplant. ADPKD patients are one of the more often qualified groups for kidney transplantation — they account for 12–15% of kidney recipients annually. In some ADPKD patients, cystic liver

Address for correspondence:
Alicja Dębska-Ślizień,
Department of Nephrology,
Transplantology and Internal
Medicine, Medical Faculty,
Medical University of Gdańsk
e-mail: adeb@gumed.edu.pl

disease predominates, which is sometimes an indication for liver transplant. The optimal form of treatment in some patients may be simultaneous kidney and liver transplantation. Many patients require their kidney to be removed before qualifying for transplantation. Qualification for nephrectomy is a complex decision-making process and is usually based on the experience of surgeons; however, the current criteria are very subjective and differ among centers. Additionally, there is a risk of blood loss and a need for blood transfusion, which immunizes the patient. All of this extends the qualification process, postpones transplantation, and prevents pre-emptive transplantation. We encounter situations where a relative of an ADPKD patient wants to become a family kidney donor, which raises dilemmas that we want to solve in this study. We paid attention to radiological aspects of kidney transplants in ADPKD patients. We also want to dispel doubts regarding the qualification of ADPKD patients for renal replacement therapy using peritoneal dialysis. Those and other issues have been addressed in the guidelines by the expert group.

TRANSPLANT CANDIDATE EVALUATION IN PATIENTS REQUIRING NEPHRECTOMY BEFORE TRANSPLANTATION

Magdalena Jankowska, Alicja Dębska-Ślizień

Due to their younger age and low comorbidity, ADPKD patients are very good candidates for kidney transplants compared to the general population of recipients. Nevertheless, preparing a patient with ADPKD for evaluation and adding them to the waitlist is sometimes associated with difficulties specific to this group of patients, including the necessary removal of one or, rarely, both of the patient's kidneys (native nephrectomy, NN). From our observations [1] and literature data [2], it seems that it might be necessary for nearly 40% of potential ADPKD recipients. Due to a lack of systematic objectification of indications, this rate remains variable depending on the experience of a given transplant center. There is no doubt, however, that this procedure should be individualized and not dealt with routinely [3].

The risk of a potential need for NN should be assessed before the phase of accelerated renal function loss when it is planned to educate the patient about the available renal replacement therapy options.

RISK ASSESSMENT FOR RAPID DISEASE PROGRESSION

There are a number of useful indicators for risk assessment of rapid ADPKD progression which help estimate the time left to make a decision about kidney transplantation and possible NN. Those indicators include clinical, genetic, radiological, biochemical, and environmental factors, which are listed in Table 1 [4]. In Europe, the risk of rapid progression is also assessed using the PROPKD (Predicting Renal Outcomes in ADPKD) score [5], and the indicators included in the guidelines by the working group on tolvaptan therapy at ERA (European Renal Association) [6]. In clinical practice, it is helpful to use kidney size on ultrasound examination exceeding 16 cm in a patient younger than 45 and/or a documented decrease in the estimated glomerular filtration rate (eGFR) of > 5 mL/min/1.73 cm^2 of the body surface area over one year as an indicator of rapid disease progression [7].

EVALUATION OF INDICATIONS FOR NEPHRECTOMY

Evaluation of indications for nephrectomy has been discussed in detail in section **Indications for nephrectomy**.

From our experience, it seems that magnetic resonance imaging (MRI) without contrast

Table 1. Indicators of rapid autosomal dominant polycystic kidney disease progression [4]

Genetic
Pathogenic variant of the gene *PKD1*
5'-truncating variant
Presence of modifying genes
Clinical
Male sex
Early age at symptom onset (including hypertension)
Early decline in the GFR
Large kidney size
Episodes of hematuria
Nephrolithiasis
Infected cyst
Radiological
Class 1C, 1D, or 1E according to Mayo classification
Large total kidney volume (TKV)
Environmental
Low water intake
High consumption of calories and sodium
Obesity
Tobacco smoking
Biochemical
High plasma copeptin concentration
Proteinuria
High urine osmolality

enhancement, recommended in the diagnosis of ADPKD with eGFR < 60 mL/min/1.73 cm^2, is helpful for objectification of indications [8]. It allows assessing not only the total kidney volume (TKV) but also the degree of cystic liver enlargement, the presence (or the number) of complicated cysts, and the enlarged kidneys compressing venous vessels, mainly the inferior vena cava.

KDIGO (Kidney Disease: Improving Global Outcomes) experts recommend abdominal and pelvic computed tomography (CT) study without contrast enhancement to determine whether it would be beneficial for the patient to undergo one- or multiple-stage nephrectomy [9].

CHOICE OF NEPHRECTOMY TIMING

It should be noted that NN excludes the possibility of pre-emptive kidney transplantation, when the patient does not have a family donor. If the transplant center has experience in simultaneous NN and kidney transplantation, such an option is possible, but it is associated with a higher complication rate (longer duration of surgery, prolonged hospital stay, necessary blood transfusion) [10, 11]. Sometimes, however, when the patient is informed about such risks, they consciously decide to choose this option if the quality of life is their priority [12]. It also seems that long-term results of such procedures do not differ from non-simultaneous operations [10–13].

Due to dialysis dependence of patients undergoing NN, it should be postponed until renal replacement therapy is initiated unless there are urgent indications for surgery. Then, hemodialysis seems to be the option of choice, however, peritoneal dialysis following NN surgery is also possible. The issues relating to peritoneal dialysis are discussed in the section **Peritoneal dialysis in a patient with ADPKD before transplantation or after the loss of function of the kidney graft**.

PREPARATION FOR NEPHRECTOMY

When NN is conducted due to emergency indications (e.g. cancer) in a patient who has not been dialyzed so far, the preparation for the procedure includes a choice of the renal replacement therapy method which will be necessary after surgery and to ensure vascular access. In patients receiving renal replacement therapy, it seems reasonable to maintain an interval of about 2–3 months from the initiation of dialysis therapy, although there are insufficient data to support this practice. It results from the observation that the first 90 days of dialysis is a period with an increased risk of complications, including death.

Unless there are contraindications, the possibility of securing blood for autotransfusion should be considered in the process of preparing for the NN surgery, which is discussed in more detail in section **Autotransfusion in a candidate for nephrectomy**.

PREPARATION FOR TRANSPLANT

The basic issue in preparing a patient requiring NN surgery for a kidney transplant is to provide them with enough time to run all the tests necessary to be included on a waitlist of potential recipients. Full preparation of the patient waiting for NN helps avoid longer than necessary delays in adding them to the waitlist. In practice, it is possible even one month after nephrectomy, therefore, the preparation of a patient requiring NN does not differ from cases when patients with ADPKD are prepared for pre-emptive transplantation.

SUMMARY

It is recommended to assess the risk of rapid progression of kidney failure in patients with ADPKD. In clinical practice, it is useful to use kidney size exceeding 16 cm on ultrasound in a patient younger than 45 years and/or a documented decrease in eGFR > 5 mL/min/min/1.73 cm^2 body surface area over a year as indicators of rapid kidney progression.

Potential indications for NN should be reviewed at the time the patient is planned to be educated on the available options for renal replacement therapy.

Securing blood for autotransfusion should be considered in preparation for NN surgery unless there are contraindications.

The fundamental issue in preparation for transplant surgery in a patient who requires NN surgery is to provide them with the right amount of time to run all the necessary tests to add them to the waitlist as a potential recipient.

REFERENCES

1. Jankowska M, Kuźmiuk-Glembin I, Skonieczny P, et al. Native nephrectomy in renal transplant recipients with autosomal dominant polycystic kidney disease. Transplant Proc. 2018; 50(6): 1863–1867, doi: 10.1016/j.transproceed.2018.02.100, indexed in Pubmed: 30056917.

2. Kanaan N, Devuyst O, Pirson Y. Renal transplantation in autosomal dominant polycystic kidney disease. Nat Rev Nephrol. 2014; 10(8): 455–465, doi: 10.1038/nrneph.2014.104, indexed in Pubmed: 24935705.
3. Rozanski J, Kozlowska I, Myslak M, et al. Pretransplant nephrectomy in patients with autosomal dominant polycystic kidney disease. Transplant Proc. 2005; 37(2): 666–668, doi: 10.1016/j.transproceed.2004.12.115, indexed in Pubmed: 15848495.
4. Messa P, Alfieri CM, Montanari E, et al. ADPKD: clinical issues before and after renal transplantation. J Nephrol. 2016; 29(6): 755–763, doi: 10.1007/s40620-016-0349-7, indexed in Pubmed: 27766568.
5. Cornec-Le Gall E, Audrézet MP, Rousseau A, et al. The PROPKD score: a new algorithm to predict renal survival in autosomal dominant polycystic kidney disease. J Am Soc Nephrol. 2016; 27(3): 942–951, doi: 10.1681/ASN.2015010016, indexed in Pubmed: 26150605.
6. Müller RU, Messchendorp AL, Birn H, et al. An update on the use of tolvaptan for autosomal dominant polycystic kidney disease: consensus statement on behalf of the ERA Working Group on Inherited Kidney Disorders, the European Rare Kidney Disease Reference Network and Polycystic Kidney Disease International. Nephrol Dial Transplant. 2022; 37(5): 825–839, doi: 10.1093/ndt/gfab312, indexed in Pubmed: 35134221.
7. Dębska-Ślizień A, Jankowska M, Nowicki M, et al. Polish Society of neprology working Group – Management of autosomal polycystic kidney disease (ADPKD) and other cystic kidney diseases [in polish]. Nefrol Dial Pol. 2019; 23: 1–15.
8. Banach-Ambroziak E, Jankowska M, Grzywińska M, et al. Application of total kidney volume and its predictive value in assessment of kidney transplant waitlist candidates with autosomal dominant polycystic kidney disease. Transplant Proc. 2020; 52(8): 2273–2277, doi: 10.1016/j.transproceed.2020.02.080, indexed in Pubmed: 32312534.
9. Chadban SJ, Ahn C, Axelrod DA, et al. Summary of the kidney disease: improving global outcomes (KDIGO) clinical practice guideline on the evaluation and management of candidates for kidney transplantation. Transplantation. 2020; 104(4): 708–714, doi: 10.1097/TP.0000000000003137, indexed in Pubmed: 32224812.
10. Skauby MH, Øyen O, Hartman A, et al. Kidney transplantation with and without simultaneous bilateral native nephrectomy in patients with polycystic kidney disease: a comparative retrospective study. Transplantation. 2012; 94(4): 383–388, doi: 10.1097/TP.0b013e31825812b9, indexed in Pubmed: 22828736.
11. Neeff HP, Pisarski P, Tittelbach-Helmrich D, et al. One hundred consecutive kidney transplantations with simultaneous ipsilateral nephrectomy in patients with autosomal dominant polycystic kidney disease. Nephrol Dial Transplant. 2013; 28(2): 466–471, doi: 10.1093/ndt/gfs118, indexed in Pubmed: 23042709.
12. Argyrou C, Moris D, Vernadakis S. Tailoring the 'perfect fit' for renal transplant recipients with end-stage polycystic kidney disease: indications and timing of native nephrectomy. In Vivo. 2017; 31(3): 307–312, doi: 10.21873/invivo.11060, indexed in Pubmed: 28438856.
13. Jänigen BM, Hempel J, Holzner P, et al. Simultaneous ipsilateral nephrectomy during kidney transplantation in autosomal dominant polycystic kidney disease: a matched pair analysis of 193 consecutive cases. Langenbecks Arch Surg. 2020; 405(6): 833–842, doi: 10.1007/s00423-020-01939-3, indexed in Pubmed: 32705344.

AUTOTRANSFUSION IN A NEPHRECTOMY CANDIDATE

Magdalena Jankowska, Hanna Suchanek

Autotransfusion (autologous transfusion) is a blood transfusion procedure where the same person is the donor and the recipient. Autotransfusion includes a preoperative collection of the patient's own blood, intraoperative hemodilution, and transfusion of the intraoperative blood salvage. The discussed recommendations apply only to the first of those procedures.

An indication for autotransfusion is a potential need for blood transfusion in a patient who may require it due to a planned surgical procedure.

One basic benefit of autotransfusion for a nephrectomy candidate is avoiding the risk associated with alloimmunization. Other benefits include avoiding the risk of viral transmission, reduction of the risk of other transfusion-related complications, and limiting allogeneic transfusions [1].

Blood transfusions may be necessary for up to 39% of open nephrectomies for multicystic kidneys and in 12% of laparoscopic surgeries [2]. Blood transfusions and the associated alloimmunization constitute the most likely cause of prolonged waiting on the waitlist of potential recipients, which has been observed in ADPKD patients undergoing nephrectomy [3]. In individual cases, this may even be the reason for disqualifying the patient as a kidney transplant recipient, which has been described, e.g. in cases of planned transplantations from family donors [2].

The principles of blood collection for autotransfusion in Poland are regulated by the provisions of the Announcement of the Minister of Health from March 6, 2019 on the requirements for good practice of collecting blood and its components, testing, preparation, storage, delivery, and transportation for organizational units of the public blood service [4].

Due to contraindications for autologous blood collection listed in Table 2, patients with chronic renal failure, particularly those receiving renal replacement therapy, are not ideal candidates for autotransfusion. Patients with ADPKD, however, are usually younger and with lower comorbidity compared to oth-

Table 2. Contraindications to autologous blood collection

Absolute
Hemoglobin concentration < 10 g/dL
Active bacterial infection
Acute coronary syndrome
Severe aortic stenosis
Poorly controlled hypertension
History of myocardial infarction
Cerebral vascular insufficiency
Epilepsy
Brain tumor
Relative
Hemoglobin level 10–11 g/dL
Positive viral infection markers for HBV, HCV, HIV, history suggestive of HTLV I/II infection
Age > 70
Pregnancy
No vascular access

HBV — hepatitis B virus; HCV — hepatitis C virus; HIV — human immunodeficiency virus; HTLV — human T-cell leukemia/lymphoma virus

Table 3. Complications and side effects of blood transfusion and autologous blood transfusion

Hypervolemia
Infection
Non-immune-mediated hemolytic transfusion reaction
Immune-mediated hemolytic transfusion reaction
Hypotension
Fever
Chills
Skin redness
Allergic reaction
Disseminated intravascular coagulation (DIC)
Air embolism
Side effects of anticoagulant infusion and other preservatives

er patients eligible for kidney transplants [5]. Additionally, to achieve target hemoglobin levels, they often require small or no doses of erythropoiesis-stimulating agents [6]. Also, hemodialysis patients demonstrate good adaptation to changes in intravascular volume, which reduces the risk of donation-related hypotension.

Qualification for preoperative blood donation is conducted by the physician qualifying for nephrectomy up to 30 days before scheduled surgery. The qualifying physician issues a referral to an appropriate blood donation center, in which they specifies the date, type of surgery, and the number of packed RBC units ordered for collection. The final decision to collect autologous blood is made by the physician of the Regional Center for Blood Donation and Blood Treatment (pol. *Regionalne Centrum Krwiodawstwa i Krwiolecznictwa*, RCKiK).

Typically, 450 mL of whole blood is collected twice. This volume allows for preparation of 2 units of RBCs and 2 units of fresh frozen plasma (FFP). Blood collections are usually conducted 14 and 7 days before the scheduled transfusion (nephrectomy). The latest donation can be done 72 hours before the scheduled transfusion. From our experience, it seems that in dialysis patients, it is beneficial to maintain a 10-day interval between donations, which enables effective stimulation of erythropoiesis by administering erythropoiesis-stimulating agents (ESA). Routine assessment of iron metabolism and adequate iron supplementation are also recommended.

Before autologous blood transfusion, a blood compatibility test must be performed.

Each blood transfusion, also autologous, is associated with potential complications (Tab. 3) [7]. Nevertheless, the risk of such complications is low (0.043%) compared to allogeneic blood transfusion [7].

Due to the risk of hypervolemia in dialysis patients, autotransfusion should not be performed unless clinically indicated (perioperative blood loss, decline in the hemoglobin level). Blood products (RBCs, FFP) that have not been used for autotransfusion cannot be used for other patients and should be disposed of.

SUMMARY

The indication for autotransfusion, i.e. a medical procedure when the donor and the recipient are the same person, is necessary blood transfusion in a patient who may require it due to scheduled surgery.

The primary benefit of autotransfusion for a nephrectomy candidate is avoidance of risks associated with alloimmunization.

REFERENCES

1. Vanderlinde ES, Heal JM, Blumberg N. Autologous transfusion. BMJ. 2002; 324(7340): 772–775, doi: 10.1136/bmj.324.7340.772, indexed in Pubmed: 11923162.
2. Chebib FT, Prieto M, Jung Y, et al. Native nephrectomy in renal transplant recipients with autosomal dominant polycystic kidney disease. Transplant Direct. 2015; 1(10): e43, doi: 10.1097/TXD.0000000000000554, indexed in Pubmed: 26981586.
3. Jankowska M, Kuźmiuk-Glembin I, Skonieczny P, et al. Native nephrectomy in renal transplant recipients with autosomal dominant polycystic kidney disease. Transplant Proc. 2018; 50(6): 1863–1867, doi: 10.1016/j.transproceed.2018.02.100, indexed in Pubmed: 30056917.

4. Obwieszczenie Ministra Zdrowia z dnia 6 marca 2019 r. w sprawie wymagań dobrej praktyki pobierania krwi i jej składników, badania, preparatyki, przechowywania, wydawania i transportu dla jednostek organizacyjnych publicznej służby krwi. Dziennik Urzędowy Ministra Zdrowia. Warszawa, dnia 7 marca 2019 r., poz. 25. http://dziennikmz.mz.gov.pl/legalact/2019/25/ (12.03.2022).
5. Eckardt KU, Möllmann M, Neumann R, et al. Erythropoietin in polycystic kidneys. J Clin Invest. 1989; 84(4): 1160–1166, doi: 10.1172/JCI114280, indexed in Pubmed: 2794053.
6. Kanaan N, Devuyst O, Pirson Y. Renal transplantation in autosomal dominant polycystic kidney disease. Nat Rev Nephrol. 2014; 10(8): 455–465, doi: 10.1038/nrneph.2014.104, indexed in Pubmed: 24935705.
7. Domen RE. Adverse reactions associated with autologous blood transfusion: evaluation and incidence at a large academic hospital. Transfusion. 1998; 38(3): 296–300, doi: 10.1046/j.1537-2995.1998.38398222875.x, indexed in Pubmed: 9563411.

INDICATIONS FOR NEPHRECTOMY

Maciej Kosieradzki, Alicja Dębska-Ślizień, Marcin Matuszewski

The data on the benefits of pre-transplant nephrectomy in ADPKD patients are conflicting, and the indications and timing are heavily discussed. It is usually reserved for two situations, i.e. when kidney transplantation could be difficult or impossible due to the size of the kidneys as they descend into the pelvis below the iliac spine; or the presence of recurrent complicated cysts which do not respond to treatment. However, it should always be taken into account that patients with ADPKD generally have preserved residual kidney function, which prevents volume overload and heart failure, and removal of even one kidney will reduce the residual kidney function by about half, which will require limited fluid intake and hence reduce the patient's quality of life. Therefore, the decision to remove a polycystic kidney should be made after reviewing all those factors.

For the sake of our study, we adopted the classification of medical evidence by the Center for Evidence-Based Medicine, Oxford (Tab. 4).

Only less than 20% of ADPKD patients require native nephrectomy (uni- or bilateral) for any indication. However in transplant recipients the percentage may reach even 40%. In the study at UCSF (University of California, San Francisco), it was true for 32 out of 171 patients, half of whom underwent simultaneous nephrectomy with transplantation, while in 7 patients nephrectomy preceded transplantation, and in 9 patients it was performed after the transplantation over the 10-year study period [3]. The authors of a relatively old study in Innsbruck point out that in a group of 99 patients, nephrectomy proved necessary in 35 patients (25 — before transplantation, 10 — after transplantation). The five-year survival of the patients and the transplant was almost 20% better in the nephrectomy group compared to the group without nephrectomy. Patients who required kidney removal after transplantation had the worst 5-year transplant survival rate (52% vs. 89% in patients who did not require nephrectomy after transplantation) [4]. Nevertheless, the authors recommend nephrectomy only for recurrent complicated cysts. In our opinion, the only valid conclusion from this study is that, when indicated, the nephrectomy should be performed before transplantation and not after transplantation although the level of evidence is quite low: 4.

A recent study from Berlin compared the outcomes of 89 nephrectomies performed before transplantation and 32 nephrectomies performed after transplantation in group 2, both kidneys were 1 kg lighter on average!).

Table 4. Classification of medical evidence by the Centre for Evidence-Based Medicine

Evidence level	Description
1A	Systematic review (with homogeneity) of randomized controlled trials
1B	Individual randomized clinical trials (with narrow confidence interval)
1C	All or none
2A	Systematic review (with homogeneity) of cohort studies
2B	Individual cohort study or low-quality randomized controlled trials (< 80% follow-up)
2C	Ecological studies, cross-sectional studies
3A	Systematic review (with homogeneity) of case-control studies
3B	Individual case-control study
4	Case-series (or low-quality cohort and case-control studies)
5	Expert opinion

The indications were similar: 55% — pain, 30% — infections, 10% — urolithiasis, and 5% — bleeding. Cancer was found in over 3% of the removed tissues in the pathology study. It seems that it was a slightly safer procedure to remove the kidney after transplantation — only 1 patient developed complication of Clavien-Dindo grade III, while in the pre-transplant nephrectomy group there were 3 complications grade III, 2 grade IV, and 3 deaths although the level of statistical significance was not achieved [5]. Probably the largest group described yet includes nearly 500 kidney transplant patients at the University of Wisconsin: 303 did not undergo nephrectomy (group 1), 27 had both kidneys removed simultaneously before transplantation (group 2), and in 161 both kidneys were removed at the time of transplantation (group 3). During the 10-year follow-up, no differences were found in survival of both patients and transplants between the groups. In the group where both kidneys were left intact, 16% of patients required nephrectomy after transplantation during the 10-year follow-up period. Renal vein thrombosis was most common (4.4%) in the group where nephrectomy was performed concurrently with transplantation (in groups 1. and 2., respectively 1.3 and 0%). In the pre-transplant nephrectomy group, the surgical site infection rate was the highest (26% vs. 11 and 5%, respectively groups 1. i 3.). The best of the early surgical complications occurred with a similar frequency in each group [6]. In 47 patients who did not undergo nephrectomy within 5 years after transplantation, cyst infections that were successfully treated with antibiotic treatment developed in 3 patients, and 2 patients had hematuria that did not require aggressive treatment. No other complications were observed [7]. The authors found no rationale for routine removal of polycystic kidneys prior to transplantation (evidence level: 4). Despite leaving the kidney, the risk of urinary tract infections is only slightly increased in kidney transplant patients with ADPKD (56% vs. 44% in the group without ADPKD), and 5-year survival of patients was slightly worse (67.5% vs. 80.1%), but it should be noted that it is a disease that affects not only kidneys but also other organs [8]. Veroux et al. compared the outcomes of 40 unilateral nephrectomies performed concurrently with kidney transplantation, 80 kidney transplants in ADPKD patients without nephrectomy, and 25 nephrectomies performed before transplantation. The authors found no differences in survival of transplants and patients (mean follow-up: 5.6 years); the perioperative complication rate was the highest in the group where nephrectomy was performed before transplantation. Patients undergoing nephrectomy before transplantation also waited longer for a transplant and, at the time of transplantation, had lower hemoglobin levels and urine outputs [9]. The authors believe that unilateral nephrectomy can be safely performed simultaneously with kidney transplantation in asymptomatic patients with no free space for transplant, and that pre-transplant nephrectomy should be limited to symptomatic cases only (strength of evidence: 3B). The Freiburg Center routinely used the technique of simultaneous ipsilateral polycystic kidney removal during transplantation [10]. It prolonged the procedure by an average of 30 minutes compared to the control (propensity score matching for the closest person at the time of transplantation), and blood transfusions were also required more often (23% vs. 7%, respectively). The mean time prolongation appears small, but it may be important given the organizational challenges of a kidney transplant from a deceased donor. Surgical and medical complications occurred at the same frequency. The survival of the patient and the transplant was also comparable (strength of evidence: 3B). Similarly, in the study by Lucas et al., unilateral concurrent nephrectomy with transplantation (n = 16) extended the duration of surgery by an average of 30 minutes, without affecting blood loss or intraoperative complications [11]. Fuller et al. obtained similar results for nephrectomies performed before transplantation, during transplantation, and after kidney transplantation, while patients were most content with the simultaneous approach. However, this procedure takes significantly longer (160 min), and patients stay in the hospital longer [3].

On the other hand, Sulikowski et al. studied a group of 21 patients after transplantation in whom the polycystic kidney(s) were not removed and observed good long-term graft function in 81% of cases, with 4 cases of asymptomatic compression of the kidney transplant by the patient's own kidney cysts, and 1 death due to generalized infection, 15 cases of cyst or lower urinary tract infections and 1 hemorrhage from a cyst. Eight patients (38%) required nephrectomy after transplantation. For comparison, in the group of 25 patients who underwent nephrectomy before transplanta-

tion, 3 of them (12%) required removal of the second native kidney after transplantation, 8 (32%) had infections on the opposite side, and 5 (20%) had surgical complications. [12]. In another publication by the same group of researchers, nephrectomy of the second kidney after transplantation was necessary in 16% of patients compared to 14% of patients who did not undergo nephrectomy; however, in the group without nephrectomy, there were more serious complications (28% vs. 17%) [13].

LAPAROSCOPIC NEPHRECTOMY

Overall, laparoscopic nephrectomy or robotic laparoscopic nephrectomy shorten the recovery period [14]; however, considering the size of the polycystic kidney, which often reaches 30 cm, the use of this method seems controversial. It should be remembered that a skin incision will be necessary at some point to get the kidney out anyway. The costs of those procedures are significant, the rate of postoperative hernias — although in a different location — is similar, and no studies are comparing open, laparoscopic, or robotic techniques. In a study on 13 patients from India, injury to the spleen capsule or pleura, intestinal obstruction, and trauma to the inferior vena cava were reported for laparoscopic access [15]. Chen et al. compared 16 patients undergoing open surgery with 15 patients undergoing laparoscopic surgery; in both groups, some procedures were performed bilaterally, but the removed kidneys were relatively small (mean < 1000 cm^3). Blood loss and duration of stay in the hospital showed in favor of laparoscopic nephrectomy in ADPKD, while other complications were similar in both groups [16]. Pfister et al. recommend that very large kidneys be removed using an open technique because the number of complications in such cases is lower although the authors make this conclusion based on the available literature and not on the data from their own study [17].

BILATERAL NEPHRECTOMY

Bilateral nephrectomy can be performed simultaneously, including the laparoscopic approach, but the duration of such procedures can sometimes be very long (nearly 4 hours) [18]. Our colleagues from Katowice reported on a group of 18 patients who underwent bilateral nephrectomy [19]. Surgical complications occurred in 45% of patients (impaired wound healing — 4, postoperative hernia — 3, chronic pain — 3, subhepatic hematoma — 2, stress ulcer — 1, subileus — 1, AV fistula thrombosis — 5). The authors concluded that this procedure is associated with a high risk of complications (evidence level: 4). An experienced team can perform bilateral laparoscopic nephrectomy simultaneously with transplantation [20, 21], but in another study, nearly 64% of patients after simultaneous bilateral nephrectomy and kidney transplantation experienced severe complications requiring reoperation [22] while blood loss and the rate of urological complications were also higher [23]. Thus, it is difficult to consider such procedures to be safe (level of evidence: 4). Also, in the study by Bromberg et al., simultaneous bilateral nephrectomy with kidney transplantation was associated with a significantly higher risk of severe intraoperative complications (10% vs. 0%), longer duration of the procedure, greater blood loss, need for transfusions and longer stay in the hospital [24]. Similar results were presented by Lucas et al. Bilateral laparoscopic nephrectomy was associated with more than double blood loss, operation time was prolonged by 2 hours, and there was a much higher risk of intraoperative complications [11]. Additionally, non-surgical sequelae of bilateral nephrectomy should be considered as well, including severe anemia, chronic hypotension, or large volume fluctuations.

The most common indications for pre-transplant nephrectomy were listed according to their frequency and discussed in detail below.

1. No free space for transplant

The space limit was the most common indication for nephrectomy in the UCSF material (50% of patients), and those procedures were performed simultaneously with kidney transplantation [3]. Renal artery embolization (level of evidence: 3A) seems to be worth considering as a treatment option. In a group of 15 patients treated at the University of Lille, successful embolization resulted in a reduction of the polycystic kidney volume from 2550 cm^3 to an average of 1680 cm^3 (by 1/3) after 3 months. There were no serious complications. After the procedure, 13 patients were qualified for transplantation, and 7 underwent transplantation by the end of the study [25]. In a larger study from Bordeaux, endovascular surgery was successful in 90% of the 76 embolized kidneys, and 65 out of 73 patients were put on the waiting list. After 3 months, volume reduction of the polycystic kidney by 40% was observed, and it was reduced

by almost 60% in the long run. Post-embolization syndrome occurred in 18.3%, and severe complications in 5%, which is a significant number of cases [26]. In peritoneal dialysis patients, there was no need for conversion to hemodialysis, and the hospital stay was shorter compared to the nephrectomy patients [27].

2. Kidney (area) pain poorly controlled with analgesics

Chronic pain in the area of an enlarged kidney was one of the most common indications for nephrectomy performed before transplantation [3]. Renal artery embolization is also an effective method of treating pain associated with renomegaly (level of evidence: 3A) [28].

3. Recurrent hematuria in patients in whom arterial embolization is unfeasible or not planned

Out of 7 patients reported by the UCSF study, who underwent pre-transplant nephrectomy, hematuria was one of the three main indications (others included suspected cancer and pain) [3].

4. Recurrent infections

Recurrent infections are the most common indication for post-transplant native nephrectomy [3] (level of evidence: 4). In an older study from Nantes (1993) on 39 patients receiving kidney transplants, 3 patients died as a result of infectious complications within 4 years of follow-up [29].

5. Suspicion of cancer

Suspicion of cancer in a polycystic kidney was one of the most common indications for nephrectomy in preparation for a kidney transplant [3]. Among the observed 954 lesions Bosniak IIF, Schoots et al. identified only 54 that ultimately required removal, and in only 9 cases cancer was confirmed [30]. However, in another study, cancer risk increased to 95% in the case of progression from type IIF to III or IV. About half of Bosniak III lesions were malignant (25–100%) [30–33]. Lesions classified as Bosniak IV were malignant on average in 90% (56–100% in individual publications).

6. Malnutrition, loss of appetite, fatigue, limited normal activity

7. Internal hernia caused by renomegaly

8. Blood transfusion

Patients, who require removal of the polycystic kidney, often show low hemoglobin levels. Due to the extensive scope of the procedure, it is necessary to secure blood, and sometimes they may require blood transfusion postoperatively. To eliminate potential immune-mediated complications associated with blood transfusion, it seems beneficial to prepare the patient's own blood for autotransfusion over a prolonged period, as described in the section above: **Autotransfusion in a nephrectomy candidate**.

Table 5. The most important challenges relating to nephrectomy which need to be considered in ADPKD patients

Recommendation	Evidence level
Routine removal of polycystic kidneys is not recommended prior to transplantation	4
Such indication may be: lack of space for the transplant due to the very large volume of the polycystic kidney, or clinically significant symptoms related to the changes in the kidney	
If the decision is made to perform a nephrectomy, the procedure can be performed a) during kidney transplantation b) before kidney transplantation	 3B 4
Renal artery embolization is a possible effective method of reducing the kidney volume when it can the size of the kidney is a contraindication to transplantation and reduces pain symptoms	3A
Simultaneous bilateral nephrectomy is associated with a higher risk of complications. Indications for such a procedure should be well defined, and the procedure itself should not be combined with kidney transplantation	4
Laparoscopic or laparoscopic robotic surgery should be limited to cases where the size of the kidney is not extremely large	4
In every patient with polycystic kidney disease, unless both kidneys are to be removed for other indications, a CT or MRI scan should be obtained at least once before transplantation to assess cancer risk	5
Bosniak IIF lesions require periodic re-evaluation, and transplantation should not be delayed	2A
Bosniak III or IV lesions require nephrectomy	2A
Before the procedure, it is recommended to secure blood for autotransfusion	

SUMMARY

The most important challenges relating to nephrectomy that need to be considered with ADPKD patients are summarized in Table 5. Indications, duration of nephrectomy, and the surgical technique should be chosen individually.

REFERENCES

1. Patel MS, Kandula P, Wojciechowski D, et al. Trends in the management and outcomes of kidney transplantation for autosomal dominant polycystic kidney disease. J Transplant. 2014; 2014: 675697, doi: 10.1155/2014/675697, indexed in Pubmed: 25165573.
2. Bretagnol A, Büchler M, Boutin JM, et al. [Renal transplantation in patients with autosomal dominant polycystic kidney disease: pre-transplantation evaluation and follow-up]. Nephrol Ther. 2007; 3(7): 449–455, doi: 10.1016/j.nephro.2007.07.002, indexed in Pubmed: 18047999.
3. Fuller TF, Brennan TV, Feng S, et al. End stage polycystic kidney disease: indications and timing of native nephrectomy relative to kidney transplantation. J Urol. 2005; 174(6): 2284–2288, doi: 10.1097/01.ju.0000181208.06507.aa, indexed in Pubmed: 16280813.
4. Brazda E, Ofner D, Riedmann B, et al. The effect of nephrectomy on the outcome of renal transplantation in patients with polycystic kidney disease. Ann Transplant. 1996; 1(2): 15–18, indexed in Pubmed: 9869924.
5. Maxeiner A, Bichmann A, Oberländer N, et al. Native nephrectomy before and after renal transplantation in patients with autosomal dominant polycystic kidney disease (ADPKD). J Clin Med. 2019; 8(10): 1622, doi: 10.3390/jcm8101622, indexed in Pubmed: 31590248.
6. Grodstein EI, Baggett N, Wayne S, et al. An evaluation of the safety and efficacy of simultaneous bilateral nephrectomy and renal transplantation for polycystic kidney disease: a 20-year experience. Transplantation. 2017; 101(11): 2774–2779, doi: 10.1097/TP.0000000000001779, indexed in Pubmed: 29064957.
7. Knispel HH, Klän R, Offermann G, et al. Transplantation in autosomal dominant polycystic kidney disease without nephrectomy. Urol Int. 1996; 56(2): 75–78, doi: 10.1159/000282815, indexed in Pubmed: 8659014.
8. Illesy L, Kovács DÁ, Szabó RP, et al. Autosomal dominant polycystic kidney disease transplant recipients after kidney transplantation: a single-center experience. Transplant Proc. 2017; 49(7): 1522–1525, doi: 10.1016/j.transproceed.2017.06.014, indexed in Pubmed: 28838432.
9. Veroux M, Zerbo D, Basile G, et al. Simultaneous native nephrectomy and kidney transplantation in patients with autosomal dominant polycystic kidney disease. PLoS One. 2016; 11(6): e0155481, doi: 10.1371/journal.pone.0155481, indexed in Pubmed: 27257690.
10. Jänigen BM, Hempel J, Holzner P, et al. Simultaneous ipsilateral nephrectomy during kidney transplantation in autosomal dominant polycystic kidney disease: a matched pair analysis of 193 consecutive cases. Langenbecks Arch Surg. 2020; 405(6): 833–842, doi: 10.1007/s00423-020-01939-3, indexed in Pubmed: 32705344.
11. Lucas SM, Mofunanya TC, Goggins WC, et al. Staged nephrectomy versus bilateral laparoscopic nephrectomy in patients with autosomal dominant polycystic kidney disease. J Urol. 2010; 184(5): 2054–2059, doi: 10.1016/j.juro.2010.06.150, indexed in Pubmed: 20850813.
12. Sulikowski T, Tejchman K, Zietek Z, et al. Experience with autosomal dominant polycystic kidney disease in patients before and after renal transplantation: a 7-year observation. Transplant Proc. 2009; 41(1): 177–180, doi: 10.1016/j.transproceed.2008.10.034, indexed in Pubmed: 19249508.
13. Rozanski J, Kozlowska I, Myslak M, et al. Pretransplant nephrectomy in patients with autosomal dominant polycystic kidney disease. Transplant Proc. 2005; 37(2): 666–668, doi: 10.1016/j.transproceed.2004.12.115, indexed in Pubmed: 15848495.
14. Dunn MD, Portis AJ, Elbahnasy AM, et al. Laparoscopic nephrectomy in patients with end-stage renal disease and autosomal dominant polycystic kidney disease. Am J Kidney Dis. 2000; 35(4): 720–725, doi: 10.1016/s0272-6386(00)70021-7, indexed in Pubmed: 10739795.
15. Desai MR, Nandkishore SK, Ganpule A, et al. Pretransplant laparoscopic nephrectomy in adult polycystic kidney disease: a single centre experience. BJU Int. 2008; 101(1): 94–97, doi: 10.1111/j.1464-410X.2007.07229.x, indexed in Pubmed: 17922857.
16. Chen K, Tan YuG, Tan D, et al. Predictors and outcomes of laparoscopic nephrectomy in autosomal dominant polycystic kidney disease. Investig Clin Urol. 2018; 59(4): 238–245, doi: 10.4111/icu.2018.59.4.238, indexed in Pubmed: 29984338.
17. Pfister D, Thüer D, Heidenreich A. [Pitfalls and outcome of nephrectomy for patients with polycystic kidney disease: Peri- and postoperative results]. Urologe A. 2010; 49(9): 1156, 1158–62, doi: 10.1007/s00120-010-2337-1, indexed in Pubmed: 20571752.
18. Desai PJ, Castle EP, Daley SM, et al. Bilateral laparoscopic nephrectomy for significantly enlarged polycystic kidneys: a technique to optimize outcome in the largest of specimens. BJU Int. 2008; 101(8): 1019–1023, doi: 10.1111/j.1464-410X.2007.07423.x, indexed in Pubmed: 18190626.
19. Król R, Ziaja J, Cierniak T, et al. Simultaneous transabdominal bilateral nephrectomy in potential kidney transplant recipients. Transplant Proc. 2006; 38(1): 28–30, doi: 10.1016/j.transproceed.2005.12.099, indexed in Pubmed: 16504655.
20. Martin AD, Mekeel KL, Castle EP, et al. Laparoscopic bilateral native nephrectomies with simultaneous kidney transplantation. BJU Int. 2012; 110(11 Pt C): E1003–E1007, doi: 10.1111/j.1464-410X.2012.11379.x, indexed in Pubmed: 22882539.
21. Kramer A, Sausville J, Haririan A, et al. Simultaneous bilateral native nephrectomy and living donor renal transplantation are successful for polycystic kidney disease: the University of Maryland experience. J Urol. 2009; 181(2): 724–728, doi: 10.1016/j.juro.2008.10.008, indexed in Pubmed: 19091353.
22. Ismail HR, Flechner SM, Kaouk JH, et al. Simultaneous vs. sequential laparoscopic bilateral native nephrectomy and renal transplantation. Transplantation. 2005; 80(8): 1124–1127, doi: 10.1097/01.tp.0000179109.51593.87, indexed in Pubmed: 16278596.
23. Tyson MD, Wisenbaugh ES, Castle EP, et al. Simultaneous kidney transplantation and bilateral native nephrectomy for polycystic kidney disease. J Urol. 2013; 190(6): 2170–2174, doi: 10.1016/j.juro.2013.05.057, indexed in Pubmed: 23727414.
24. Ahmad SB, Inouye B, Phelan MS, et al. Live donor renal transplant with simultaneous bilateral nephrectomy for autosomal dominant polycystic kidney disease is feasible and

satisfactory at long-term follow-up. Transplantation. 2016; 100(2): 407–415, doi: 10.1097/TP.0000000000000838, indexed in Pubmed: 26262506.
25. Saljoghi R, Le Vourch A, Renard B, et al. [Arterial embolization of polycystic kidneys as an alternative to ergonomic nephrectomy in renal pre-transplantation. Monocentric retrospective study]. Prog Urol. 2019; 29(10): 482–489, doi: 10.1016/j.purol.2019.07.005, indexed in Pubmed: 31383509.
26. Petitpierre F, Cornelis F, Couzi L, et al. Embolization of renal arteries before transplantation in patients with polycystic kidney disease: a single institution long-term experience. Eur Radiol. 2015; 25(11): 3263–3271, doi: 10.1007/s00330-015-3730-3, indexed in Pubmed: 25981217.
27. Pierre M, Moreau K, Braconnier A, et al. Unilateral nephrectomy versus renal arterial embolization and technique survival in peritoneal dialysis patients with autosomal dominant polycystic kidney disease. Nephrol Dial Transplant. 2020; 35(2): 320–327, doi: 10.1093/ndt/gfz200, indexed in Pubmed: 31747008.
28. Ye W, Voss MD, Athreya S. Volume reduction in enlarged kidneys in autosomal dominant polycystic kidney disease (ADPKD) prior to renal transplant with transcatheter arterial embolization (TAE): a systematic review and meta-analysis. Cardiovasc Intervent Radiol. 2018; 41(6): 828–834, doi: 10.1007/s00270-018-1890-7, indexed in Pubmed: 29388019.
29. Wetzel O, Hormi M, Le Normand L, et al. [Autosomal dominant polycystic kidney disease: urologic complications and results of kidney transplantation: 217 patients]. Prog Urol. 1993; 3(2): 252–262, indexed in Pubmed: 8508209.
30. Schoots IG, Zaccai K, Hunink MG, et al. Bosniak classification for complex renal cysts reevaluated: a systematic review. J Urol. 2017; 198(1): 12–21, doi: 10.1016/j.juro.2016.09.160, indexed in Pubmed: 28286071.
31. Smith AD, Allen BC, Sanyal R, et al. Outcomes and complications related to the management of Bosniak cystic renal lesions. AJR Am J Roentgenol. 2015; 204(5): W550–W556, doi: 10.2214/AJR.14.13149, indexed in Pubmed: 25905961.
32. Mousessian PN, Yamauchi FI, Mussi TC, et al. Malignancy rate, histologic grade, and progression of bosniak category III and IV complex renal cystic lesions. AJR Am J Roentgenol. 2017; 209(6): 1285–1290, doi: 10.2214/AJR.17.18142, indexed in Pubmed: 28981360.
33. Hindman NM. Cystic renal masses. Abdom Radiol (NY). 2016; 41(6): 1020–1034, doi: 10.1007/s00261-016-0761-4, indexed in Pubmed: 27154722.

INDICATIONS FOR LIVER TRANSPLANT IN CYSTIC LIVER DISEASE IN PATIENTS WITH ADPKD INDICATIONS AND QUALIFICATIONS FOR ONE-STEP LIVER AND KIDNEY TRANSPLANT

Krzysztof Zieniewicz, Alicja Dębska-Ślizień, Magdalena Durlik

Polycystic liver disease (PLD) may occur in isolation or, more commonly, may be an extra-renal manifestation of ADPKD. This disease is the most common extra-renal symptom of ADPKD and affects over 80% of adult ADPKD patients [1]. Regardless of this, isolated liver cysts may be a symptom of autosomal dominant polycystic liver disease (ADPLD), which is a rare genetic disease not related to mutations in the *PKD1* and *PKD2* genes.

The risk factors of PLD in ADPKD include the following: age, female sex, previous pregnancies, exogenous estrogen replacement therapy, and significant TKV [1, 2]. There is a consensus that women with symptomatic PLD should not use hormonal contraceptives or hormone replacement therapy. Not only estrogens are harmful, but so is progesterone because, like estrogens, it promotes proliferation of cholangiocytes.

Most PLD patients do not experience any symptoms, and even when PLD is significantly advanced, liver function is not compromised. However, about 20% of patients experience symptoms of abdominal compartment syndrome. Severe hepatomegaly causes compression of adjacent organs, i.e. stomach, lungs, and intestines, which may cause back pain, abdominal pain, vomiting, belching, feeling of fullness, gastrointestinal reflux, loss of appetite, weight loss, cachexia, sarcopenia, and a significant reduction in the quality of life. A large liver mass may cause compression of the portal vein, portal hypertension, compression of the hepatic veins, and hence Buddha-Chiari syndrome, compression of the inferior vena cava leading to peripheral edema and ascites [1]. Figure 1 shows the size of the liver in a PLD patient.

Liver imaging assessing the severity of PLD should be a part of the initial evaluation of a patient with ADPKD. In the HALT study, PLD was evaluated based on the liver volume on MRI standardized by the patient's height, and further classified as: mild (< 1000 mL/m), medium (1000–1800 mL/m), or severe (> 1800 mL/m) [3].

Hemorrhage or infection of the cysts occur in 5% of patients causing acute abdominal pain, and they require treatment similar to that of corresponding renal complications.The basic imaging examination in this situation is ultrasound, which may be decisive in the case of strongly expressed clinical symptoms and good visualization conditions, enabling evaluation. When a complicated cyst is suspected, an abdominal CT or MRI is recommended.

In severe PLD cases (causing symptoms of abdominal compartment syndrome), pharmacotherapy is not used except for clinical trials, in which attempts have been made to use

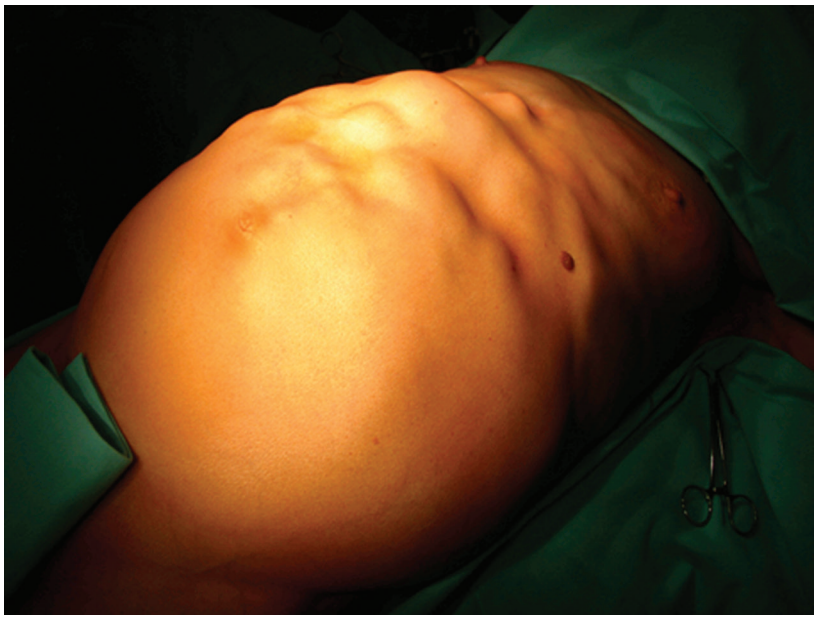

Figure 1. Polycystic liver disease. The photo was taken before liver transplantation

somatostatin analogs (octreotide, lanreotide) and sirolimus [4–6]. The reduction in liver weight was not sustained and treatment was associated with side effects, which discouraged further clinical trials. Treatment with tolvaptan is ineffective in PLD because liver cells lack V2 receptors.

Therefore, the mainstay of therapy in patients with severe symptomatic PLD is surgery, with the following surgical options: cyst fluid aspiration, fluid drainage, sclerotherapy, fenestration, embolization of the branch of the hepatic artery which provides blood supply to the largest cysts, partial liver resection, and liver transplant. Surgical interventions in PLD may be associated with complications such as bleeding, infection, bile leak, peritonitis, and above all — when carried out incorrectly — it may lead to the patient being disqualified from a liver transplant. Therefore, those procedures should be performed in experienced centers, after a careful review of indications.

LIVER TRANSPLANT IN POLYCYSTIC LIVER DISEASE

Orthotopic liver transplant (OLT) in PLD is the ultimate therapeutic option. It applies to patients, in whom partial liver resection cannot be performed or proved unsuccessful. In patients with severe PLD, the liver function is usually normal; there is no increase in liver dysfunction markers or clinical symptoms of cirrhosis. Neither the MELD (Model for End Stage Liver Disease) system, in which the bilirubin, creatinine, international normalized ratio (INR), and serum sodium levels are used to calculate the score, nor the Child-Pugh score (encephalopathy, ascites, bilirubin, INR, albumin) reflect the severity of PLD. Hence organ allocation based on those scores gives little chance for OLT in PLD patients. As a result, most patient allocation systems with PLD add exception points. This sometimes raises ethical dilemmas as to whether it is justified to expose patients to immunosuppressive treatment for the rest of their lives just to improve their quality of life.

However, indications for OLT in PLD patients include massive hepatomegaly combined with malnutrition, low serum albumin, and sarcopenia, or recurrent serious complications such as infected or ruptured cysts, hemorrhage, and portal hypertension. Those symptoms not only reduce the quality of life but also can be fatal in the long run. Liver transplantation corrects malnutrition or cachexia and improves the patient's quality of life. A concurrent kidney transplant is not necessary if there is no evidence of kidney failure, and it can usually be postponed for many years.

In PLD patients, hepatectomy preceding OLT may be difficult due to possible multiple adhesions; this also applies to patients following previous partial hepatectomy. Figure 1 shows the situation before liver transplantation, and Figure 2 shows a picture taken intraoperatively during hepatectomy.

The results of OLT in patients with PLD are comparable to the results in recipients with hepatic failure of other etiologies [7–15]. Based on the data from the European Liver Transplant Registry (ELTR) and American registries, as well as reports from the literature from Asian countries, OLT is an effective method of treatment in patients with PLD, with very good long-term survival — from over 90% (one year) through 85–90 % (5 years) to 77% (10 years) [10, 13].

INDICATIONS AND QUALIFICATION FOR SIMULTANEOUS KIDNEY-LIVER TRANSPLANT

Qualification for simultaneous liver-kidney transplantation (SLKT) should be interdisciplinary and include consultation with a hepatologist, nephrologist, and transplant surgeon. Submission to the national waiting list should include medical data on eligibility for transplantation of both organs.

The indication for a kidney transplant in ADPKD is end-stage renal failure. A pre-emp-

tive kidney transplant together with a liver transplant is an optimal approach if the latter is also indicated. The eGFR value at which the patient should be considered for SLKT is < 30 mL/min/1.73 cm^2. The SLKT can also be performed in an already dialyzed patient. The assessment of all systems and organs is the same as in the case of only kidney transplant. Abdominal imaging is essential, ideally with MRI.

The Organ Procurement and Transplant Network (OPTN) suggests that the following rules should be taken into account when qualifying a patient with cirrhosis for SLKT [16]:

1. chronic kidney disease (defined as eGRF ≤ 60 mL/min/1.73 cm^2 for at least 90 days) and at least one of the following:
   — the last eGFR value ≤ 30 mL/min/1.73 cm^2,
   — commencing dialysis due to end-stage renal failure.
2. acute kidney injury (AKI) documented by one of the following events lasting for 6 successive weeks (documented every seven days):
   — necessary dialysis,
   — eGFR ≤ 25 mL/min/1.73 cm^2.

PLD patients have been included in the first point provided that the indication is not liver cirrhosis but rather severe symptoms of abdominal compartment syndrome. As PLD patients do not show signs of liver failure, abdominal imaging and determining the absolute indications for hepatectomy are of great importance. Removal of a kidney in a patient qualified for SLKT may change the topography inside the abdominal cavity and ameliorate symptoms of abdominal compartment syndrome. However, the presence of additional serious complications of PLD such as recurrent cyst infections, cyst ruptures, hemorrhage, and portal hypertension, favor SLKT.

In the case of SLKT, according to the allocation rules, the liver recipient receives the kidney from the same donor.

In accordance with the rules of kidney allocation of January 1, 2016 by Poltransplant, the parameters for selecting the kidney recipient are as follows: recipient of a simultaneous kidney and other organ transplants; selection of the recipient according to the rules of the transplant center, no cross-match is required; the transplant is obligatory.

Human leukocyte antigens (HLA) are determined in the recipient added to the kidney transplant waitlist, and possible immunization is evaluated with PRA (panel reactive antibody) testing, and, finally, anti-HLA is tested as well, but cross-matching with a serological method (CDC-CM, complement-dependent cytotoxicity crossmatch) is left optional for the transplant center. SLKT is most commonly performed based on blood group compatibility without crossmatching. However, a virtual crossmatch is also possible where the results are obtained almost immediately.

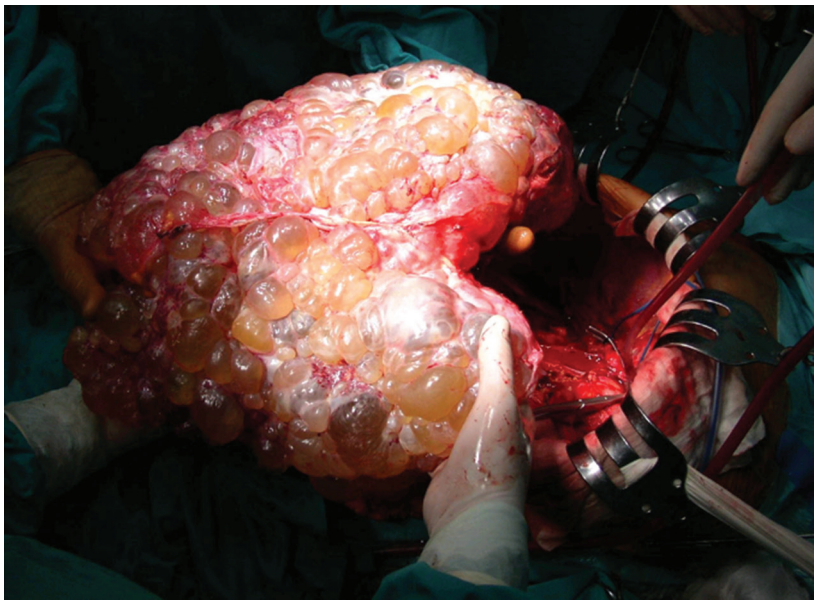

Figure 2. Polycystic liver disease. Intraoperative photo during hepatectomy

IMMUNOSUPPRESSION FOLLOWING SLKT

The SLKT procedure is most often performed based on the compatibility of blood groups without taking into account the crossmatch and the degree of immunization of the recipient. However, retrospective immunological evaluation of the recipient is possible when pre-transplant recipient serum samples are preserved. The liver exerts an immunosuppressive effect, which reduces the risk of kidney rejection. After SLKT, the disappearance or decrease of the donor-specific antibodies (DSA) can be observed (applies to DSA class I). The protective effect of the liver is related to the absorption of the preformed DSA by its reticuloendothelial system. However, an increased risk of antibody-dependent renal rejection, liver rejection, and death has been reported in recipients with class II preformed or *de novo* DSA antibodies [17]. The protective effect of the liver is also not observed in the case of kidney transplantation in a previous liver recipient.

No specific recommendations have been made regarding the immunosuppressive regi-

men in SLKT recipients. As delayed graft function (DGF) is one of complications observed after SLKT, it has been proposed to use induction therapy with monoclonal antibodies (anti-IL2R), mycophenolate mofetil, and glicocorticoids and to postpone the initiation of tacrolimus by 2 days. In patients undergoing elective transplantation, when it is possible to determine the degree of recipient immunization and, in immunized patients, polyclonal antibodies (ATG, anti-thymocyte globulin) should be considered instead of anti-IL2R antibodies [18].

The patient's survival was better in SLKT compared to OLT [19, 20]. However, in patients with significant comorbidity, cardiovascular risk, previous history of sepsis, prolonged OLT surgery, or instability during OLT, the risk associated with SLKT is significant and treatment should be limited to liver transplantation.

SUMMARY

Polycystic liver disease is the most common extra-renal symptom of ADPKD and occurs in over 80% of adult ADPKD patients. Isolated liver cysts can also be a symptom of another rare genetic disease called ADPLD. In patients with severe PLD, liver function is usually normal; there is no increase in markers of liver dysfunction or clinical symptoms of cirrhosis. Nevertheless, OLT in PLD patients with symptoms of abdominal compartment syndrome can be a life-saving procedure and can improve the patient's quality of life.

In PLD patients with renal failure, SLKT should be considered.

REFERENCES

1. Chapman AB, Devuyst O, Eckardt KU, et al. Conference Participants. Autosomal-dominant polycystic kidney disease (ADPKD): executive summary from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. Kidney Int. 2015; 88(1): 17–27, doi: 10.1038/ki.2015.59, indexed in Pubmed: 25786098.
2. Bae KT, Zhu F, Chapman AB, et al. Consortium for Radiologic Imaging Studies of Polycystic Kidney Disease (CRISP). Magnetic resonance imaging evaluation of hepatic cysts in early autosomal-dominant polycystic kidney disease: the Consortium for Radiologic Imaging Studies of Polycystic Kidney Disease cohort. Clin J Am Soc Nephrol. 2006; 1(1): 64–69, doi: 10.2215/CJN.00080605, indexed in Pubmed: 17699192.
3. Hogan MC, Abebe K, Torres VE, et al. Liver involvement in early autosomal-dominant polycystic kidney disease. Clin Gastroenterol Hepatol. 2015; 13(1): 155–164.e6, doi: 10.1016/j.cgh.2014.07.051, indexed in Pubmed: 25111236.
4. Gevers TJG, Hol JC, Monshouwer R, et al. Effect of lanreotide on polycystic liver and kidneys in autosomal dominant polycystic kidney disease: an observational trial. Liver Int. 2015; 35(5): 1607–1614, doi: 10.1111/liv.12726, indexed in Pubmed: 25369108.
5. Pisani A, Sabbatini M, Imbriaco M, et al. ALADIN Study Group. Long-term effects of octreotide on liver volume in patients with polycystic kidney and liver disease. Clin Gastroenterol Hepatol. 2016; 14(7): 1022–1030.e4, doi: 10.1016/j.cgh.2015.12.049, indexed in Pubmed: 26844873.
6. Qian Qi, Du H, King B, et al. Sirolimus reduces polycystic liver volume in ADPKD patients. J Am Soc Nephrol. 2008; 19(3): 631–638, doi: 10.1681/asn.2007050626, indexed in Pubmed: 18199797.
7. van Aerts RMM, van de Laarschot LFM, Banales JM, et al. Clinical management of polycystic liver disease. J Hepatol. 2018; 68(4): 827–837, doi: 10.1016/j.jhep.2017.11.024, indexed in Pubmed: 29175241.
8. Dios-Barbeito S, Domínguez-Bastante M, Moreno-Navas A, et al. Multicentric study of the andalusian experience in polycystic liver disease as indication for liver transplantation. Transplant Proc. 2018; 50(2): 613–616, doi: 10.1016/j.transproceed.2017.09.073, indexed in Pubmed: 29579867.
9. Gedaly R, Guidry P, Davenport D, et al. Peri-operative challenges and long-term outcomes in liver transplantation for polycystic liver disease. HPB (Oxford). 2013; 15(4): 302–306, doi: 10.1111/j.1477-2574.2012.00579.x, indexed in Pubmed: 23458516.
10. van Keimpema L, Nevens F, Adam R, et al. European Liver and Intestine Transplant Association. Excellent survival after liver transplantation for isolated polycystic liver disease: an European Liver Transplant Registry study. Transpl Int. 2011; 24(12): 1239–1245, doi: 10.1111/j.1432-2277.2011.01360.x, indexed in Pubmed: 21955068.
11. Durazo FA, Tong MJ. Unusual indications for transplantation. In: Busuttil R, Klintmalm G. ed. Transplantation of the Liver. 3rd Edition. Elsevier/Saunders, Philadelphia 2015. 256–267.
12. Ruiz R, Klintmalm G. Combined liver-kidney transplantation. In: Busuttil R, Klintmalm G. ed. Transplantation of the Liver. 3rd Edition. Elsevier/Saunders, Philadelphia 2015. 793–800
13. Ding F, Tang H, Zhao H, et al. Long-term results of liver transplantation for polycystic liver disease: Single-center experience in China. Exp Ther Med. 2019; 17(5): 4183–4189, doi: 10.3892/etm.2019.7449, indexed in Pubmed: 31007749.
14. Bari K, Sharma P. Optimizing the selection of patients for simultaneous liver-kidney transplant. Clin Liver Dis. 2021; 25(1): 89–102, doi: 10.1016/j.cld.2020.08.006, indexed in Pubmed: 33978585.
15. Alsager M, Neong SF, Gandhi R, et al. Liver transplantation in adult polycystic liver disease: the Ontario experience. BMC Gastroenterol. 2021; 21(1): 115, doi: 10.1186/s12876-021-01703-x, indexed in Pubmed: 33750299.
16. Miles CD, Westphal S, Liapakis A, et al. Simultaneous liver-kidney transplantation: impact on liver transplant patients and the kidney transplant waiting list. Curr Transplant Rep. 2018; 5(1): 1–6, doi: 10.1007/s40472-018-0175-z, indexed in Pubmed: 29564203.
17. O'Leary JG, Gebel HM, Ruiz R, et al. Class II alloantibody and mortality in simultaneous liver-kidney transplantation. Am J Transplant. 2013; 13(4): 954–960, doi: 10.1111/ajt.12147, indexed in Pubmed: 23433356.

18. Das A, Taner T, Kim J, et al. Crossmatch, donor-specific antibody testing, and immunosuppression in simultaneous liver and kidney transplantation: a review. Transplantation. 2021; 105(12): e285–e291, doi: 10.1097/TP.0000000000003694, indexed in Pubmed: 33606486.
19. Coquillard C, Berger J, Daily M, et al. Combined liver-kidney transplantation for polycystic liver and kidney disease: analysis from the United Network for Organ Sharing dataset. Liver Int. 2016; 36(7): 1018–1025, doi: 10.1111/liv.13041, indexed in Pubmed: 26663575.
20. Fong TL, Khemichian S, Shah T, et al. Combined liver-kidney transplantation is preferable to liver transplant alone for cirrhotic patients with renal failure. Transplantation. 2012; 94(4): 411–416, doi: 10.1097/TP.0b013e3182590d6b, indexed in Pubmed: 22805440.