

SHORT THESIS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY (PHD)

Surgical complications of kidney transplantation - with special regard to the different ureteral suture techniques and the surgical aspects of autosomal dominantly inherited polycystic kidney disease

by Lóránt Illésy, MD

Supervisor: Balázs Áron Nemes, MD, PhD



UNIVERSITY OF DEBRECEN
DOCTORAL SCHOOL OF CLINICAL MEDICINE

DEBRECEN, 2025

Surgical complications of kidney transplantation - with special regard to the different ureteral suture techniques and the surgical aspects of autosomal dominantly inherited polycystic kidney disease

By Lóránt Illésy, MD

Supervisor: Balázs Áron Nemes, MD, PhD

Doctoral School of Clinical Medicine University of Debrecen

Head of the Defense Committee:	Prof. József Balla, MD, PhD, DSc, MHAS
Reviewers:	Katalin Pető, MD, PhD Gábor Telkes, MD, PhD
Members of the Defense Committee:	Prof. Béla Juhász, MD, PhD Eszter Mán, MD, PhD

The PhD Defense takes place at the Lecture Hall of Bldg. A, Department of Internal Medicine, Faculty of Medicine, University of Debrecen, on 4th of March, 2025 at 13:00

INTRODUCTION

Kidney transplantation provides a solution for patients with end-stage renal failure, which has additional benefits for both society and the patient compared to kidney replacement treatments. After the kidney transplant, it is possible to work regularly again, the possibility of having children improves, and it will also be possible to play sports, thereby regaining the joy of movement and its positive effects on physical and mental health.

The kidney transplant program has been operating in Hungary for 50 years, in Debrecen for 32 years. The number of kidney transplants nationwide is around 300 per year, of which 15% take place in Debrecen. The first kidney transplant was performed at the Surgery Clinic of the University of Debrecen on June 27, 1991, thus starting the kidney transplant program in Debrecen. Before the start of the program, in North-East Hungary, if a patient had to be transplanted, the patient was referred to either Szeged or Budapest. Starting with his first transplant in 1991, chief physician László Asztalos led the kidney transplantation surgery he built for 22 years, during his work he performed almost 840 kidney transplants, six of which were living donors. Balázs Nemes took over the leadership of the Transplantation Department in 2013, the same year Hungary joined Eurotransplant. The organization brings together 77 organ transplant centers in 8 countries. Since we joined, hyperimmunized patients have a better chance, and the time spent on the waiting list has decreased. With a proper protocol, excellent results can be achieved and this increases transplantation activity. At our university, since 2013, a paradigm shift has taken place in the Transplantation Department in many areas, in the areas of immunosuppression and aftercare. It was also a novelty that, in addition to ureteral anastomoses of the uretero-neocystostomy type, uretero-ureterostomy also became a practice. In our research, we examine in detail the surgical aspects of kidney transplantation in kidney transplant patients at the Department of Surgery of the University of Debrecen Clinical Center (DE KK). This includes detailed surgical techniques for organ removal, organ transplantation, including kidney transplantation, as well as perioperative tasks. Numerous complications affecting the transplanted kidney may develop, which may be immunological, internal medicine, surgical, or oncological in nature. All have an impact on graft and patient survival, as well as patient quality of life. In the course of our work, we discuss how autosomal dominantly inherited polycystic kidney disease affects the outcome of kidney transplantation and what surgical complications can be associated with it. Surgical complications are those complications related to surgery, the development of which may require further surgical treatment or intervention. The definition of a surgical complication was clarified by Dindo D.

and Clavien PA: "Any deviation from the ideal postoperative course, which is not characteristic of an intervention and does not mean a failure of healing". Clavien PA and his colleagues have created a 1-4 classification for complications occurring during organ transplants, starting with mild complications that do not require intervention, Grade 1, and Grade 4, which means graft loss and death. We also processed the topic at our Institute. In our research published in 2021, we categorized surgical complications occurring in kidney transplant recipients according to the level of intervention that the developed complication required.

The direction of our research was determined by the results of our study on bacterial infections after kidney transplantation. Based on these, the focus was on the comparison of ureter suture techniques, in addition to the examination of other surgical complications.

OBJECTIVE

The main goal of our research was to investigate the surgical complications of kidney transplants in Debrecen, with particular attention to the study of different techniques of ureteric suture and the examination of recipients suffering from autosomal dominantly inherited polycystic kidney disease. Our intention was and is to further promote the uniform quality assurance approach that has been systematically built at our Clinic since 2013, to search for correlations between individual surgical techniques and complications, and to examine their effect on patient and graft survival. With the research we have done, we have formulated the following goals.

1. To analyze, as a first step, the incidence of surgical complications related to kidney transplantation in the Debrecen Kidney Transplantation Program, with particular focus on the complications associated with different ureteral anastomosis techniques.
2. To investigate and determine whether there is a difference in complications between the techniques of uretero-ureterostomy and uretero-neocystostomy.
3. To identify the therapeutic options employed in our clinic for complications related to ureteral anastomosis.
4. To clarify the justification for the use of double J stents during ureteral anastomosis.
5. To study recipients suffering from autosomal dominant polycystic kidney disease, due to symptoms mimicking gastrointestinal-origin acute abdominal conditions.
6. To assess the necessity of removing polycystic kidneys and determine the optimal timing for nephrectomy in relation to the date of kidney transplantation.

PATIENTS AND METHODS

Ureteral anastomoses suture techniques

Used patient material and data usage

In our research, we retrospectively used the data of kidney transplant patients at DE KK Surgical Clinic between 2010 and 2020 (n=433). The minimum follow-up period was 12 months. During our study, we focused on those complications related to ureteral anastomosis (UAcomp) that required urological, radiological or surgical intervention after kidney transplantation. The UAcomp+ group was compared to the UAcomp- group, depending on whether a complication involving the ureteral anastomosis requiring intervention occurred. Based on literature data, donor and recipient demographic data, underlying recipient diabetes mellitus, basic immunosuppressive therapy, cold ischemic time (CIT), late graft function (DGF), urinary tract infection (UTI), and the use of ureteral catheters were compared between the two in a group. We have been performing uretero-ureterostomy (UU) since 2013, before that only uretero-neocystostomy (UNS) was performed. When selecting the sample, we took into account that the distribution of the two ureteral suture techniques should be similar, so in the examined time period, 221 kidney transplants were performed using the UNS technique, while 212 cases were performed using the UU technique. We separately examined the effect of the reconstruction techniques performed during reoperation on patient and allograft survival.

We examined the effect of the BK virus (BKV) on the development of ureteral stricture in a small sample of patients (January 2020 - January 2021, n=46). Since 2020, blood and urine samples have been taken routinely in the 3rd, 6th and 12th postoperative months in the care of kidney transplant patients. The presence of BKV in the samples is shown by polymerase chain reaction (PCR).

Definitions

- UAcomp+ and UAcomp- groups: The group of patients who required urological, radiological, or surgical intervention in connection with the ureteral anastomosis after kidney transplantation was named the UAcomp+ group. The control group was UAcomp, where no such complication occurred. Cases where the complications resolved spontaneously were excluded.
- Delayed graft function (DGF): hemodialysis is required in the first postoperative week after kidney transplantation.

- Urinary tract infection (UTI): those cases were considered UTIs that were accompanied by symptoms (fever, painful urination), bacteria were visible in the urine sediment test, which was confirmed by culture and intravenous antibiotic therapy had to be used during ward placement. We did not consider asymptomatic cases of UTI, in which the culture result of the urine sample taken on an outpatient basis showed a bacteria count of less than 10^5 .
- Use of a ureteral stent: from 1991 to 2013, only the UNS technique was used at our Clinic, which was splinted with a uretero-epicystostomy catheter in selected cases. One end of the catheter ends in the pyelon of the donor kidney, then passing through the UNS, it is pierced from the bladder and ends through the skin in the suprapubic region. Since 2013, at the same time as the introduction of UU, the use of the double J catheter has become widespread and has slowly replaced the epicystotomy catheter. Double J stents have one end in the pyelon of the donor kidney and the distal end in the bladder.
- Basic (or base) immunosuppression: The immunosuppression that starts after kidney transplantation is called basic immunosuppression, which is usually tacrolimus (TAC), mycophenolate mofetil (MMF) and steroids. Induction therapy is a separate entity.
- Induction therapy: taking into account the immunological risk of the recipient, in some cases the use of basiliximab or antithymocyte globulin.

Statistical methods

The SPSS 28.0 program (IBM, Armonk, NY, United States) was used to collect and analyze the data. The Mann-Whitney U test was used to analyze independent samples and continuous variables. A chi-square test with Fischer's exact test was used to compare categorical data. Kaplan-Meier curve with log-rank test was used to examine patient and graft survival. Normally distributed data are given as mean \pm standard deviation, non-normally distributed data as median and range. The significance level was defined as $p < 0.05$ for all statistical methods.

Autosomal dominant polycystic kidney disease

Used patient material, methods

At the Department of Surgery of the Medical and Health Sciences Center of the University of Debrecen (formerly known as the Center for Medical and Health Sciences), we retrospectively collected data on kidney transplant patients from medical records and the electronic patient documentation database (MedSolution) between 1991 and 2010. This meant a total of 734 cases. We divided the patients into two groups according to whether the cause of end-stage renal failure was autosomal-dominant polycystic kidney disease (ADPKD) or not: ADPKD and

non-ADPKD. A patient was included in the ADPKD group when he had a history of polycystic kidney confirmed by ultrasound and/or computed tomography and a family history of ADPKD. 80 patients were included in the ADPKD group. We examined the characteristics of the patients in the ADPKD group by assessing the proportion of the following characteristics: gender, age, diabetes, hypertension, immunosuppressive therapy. We analyzed the effect of ADPKD on patient and graft survival, as well as demographic data such as age, gender, and body mass index, in the entire study population. With regard to the special surgical aspects of the disease, we separately examined the frequency and correlation of colonic perforation due to diverticulosis and consequent acute abdominal symptoms with the presence of ADPKD in the entire population. Cases related to the removal of polycystic kidneys were examined separately in relation to the time of kidney transplantation.

Statistical analysis

The statistical analysis was performed with SPSS 22.0 software. Continuous variables were indicated by their median (maximum-minimum), and categorical variables were indicated as absolute numbers by specifying their percentage values. Continuous variables were compared with a two-sample t-test, for categorical variables we used a chi-square test. Kaplan-Meier analysis with a log rank test was used to determine the survival rate. The significance level for all statistical tests was $p < 0.05$.

RESULTS

Results in an analysis of suture techniques for ureteral anastomosis

Risk factors of complications related to ureteral anastomosis and examination of the possibility of interventions

In the examined 10-year time period, among 433 kidney transplant patients, the rate of (total) complications requiring surgical, urological, or interventional radiological intervention was 21.1% (n=96). 41.7% (n=40) of the complications, i.e. 9.2% in total, were complications related to ureteral anastomosis (UAcomp). The proportion of surgical and non-surgical interventions was equal, 67.5% (n=27). 48.1% (n=13) of the patients with complications were treated conservatively, but 51.9% (n=14) had to undergo reoperation ($p<0.001$). The 27 cases in which reoperation was performed due to UAcomp represented 6.2% of the entire examined population. The distribution of suture techniques for ureteral anastomoses was as follows: 51.0% (n=221) UNS and 49.0% (n=212) UU. The rate of complications (Uacomp) involving the ureter was 10.9% (n=24) with the UNS technique, and 7.5% (n=16) with the UU technique ($p=0.184$). For a given patient, more than one intervention could occur if the primary intervention was unsuccessful. The first therapeutic response to be chosen was always the minimally invasive solution. If a milder picture was obtained during the diagnosis, then a urological intervention was used. In cases where reoperation was the only solution, we immediately took the patient to surgery at the time of diagnosis, without urological intervention. The most common technique during reoperations after the resection of the damaged ureteral segment was UNS with 37.0% (n=10), but for the re-sewn anastomosis, we also used UU (11.1%; n=3), pyelo-ureterostomy (7, 4%; n=2), and pyelo-neocystostomy (11.1%; n=3), depending on the surgical situation. In 22.2% of the cases (n=6), only an additional filling was inserted due to leakage of urine, typically in UNS cases. The type of interventions did not correlate significantly with the ureteral suture technique.

In two cases, we were eventually forced to undergo graftectomy due to UAcomp. This is a very good rate, since only 0.4% of patients lost their kidneys in the early period directly due to ureteral complications. Both cases occurred in the 3rd postoperative month, the primary anastomoses were UU and UNS in a 1:1 ratio. The picture is colored by the fact that one of the graftectomies was a horseshoe kidney with a double ureter (UU technique). In the immediate postoperative period, a DJ stent was inserted due to signs of minimal urinary leakage. After that, the patient was discharged home with good graft function and adequate diuresis. Finally,

after the removal of the DJ stent, a graftectomy was performed due to urosepsis. In the other case, where a graftectomy was finally performed, the primary ureteric suture was UNS, and the patient was reoperated twice due to necrosis of the ureter and leakage of urine. Finally, due to recurrent UTI and urosepsis after the 3rd postoperative month, we removed the kidney allograft.

There was no significant correlation between the UAcomp and the examined donor and recipient demographic parameters, just as the type of immunosuppression and the cold ischemia time (CIT) did not significantly worsen the outcome. The rate of diabetes was almost twice as high in the complication population, but the value was not yet significant. Delayed graft function (DGF) is more common in the UAcomp+ group than in the UAcomp- group, but the correlation is not significant ($p=0.411$). 67.5% of the UAcomp+ group developed a UTI, compared to only 29.5% of the UAcomp- group ($p<0.001$). The rate of use of a ureteric catheter during the preparation of the ureteral anastomosis was lower in the group with later complications (65.0%) than in the uncomplicated group (92.1%). This was considered significant ($p<0.001$). The protective effect of ureteral splinting can be assumed. 33.0% of the studied population ($n=143$) were treated in the hospital ward for urinary infection, and this rate was significantly higher in the UAcomp+ group than in the UAcomp- group (67.5% vs. 29.0%; $p<0.001$).

The proportion of UAcomp+ cases changes during certain periods of the kidney transplant center in Debrecen. Presumably, the increase in experience may explain the decrease in the rate of complications. In the first sub-period (2010-2013), UNS was the only suture technique, which was predominantly performed by an experienced surgeon. The second sub-period (2014-2017) was characterized by an increase in the number of cases, and the UU suture technique was introduced in addition to the UNS. The new technique was mastered by the young surgical colleagues during this period. In the last subperiod (2018-2020), the application of both suture techniques was made with more experienced hands. This result therefore confirms an important point, that it leads to a reduction in the rate of complications if a dedicated team, trained on the basis of common professional principles (with a school-creating nature), performs surgeries in a specialty.

Association between ureteral suture technique and complication of ureteral anastomosis

The insufficiency of the ureteral suture can basically have two manifestations, the leakage of urine or the narrowing of the ureter. In the early period, the narrowing of the ureter can be caused by an error in the suturing technique, scarring, or a blood supply disorder or breakage of

the donor ureter that has been left too long. At the level of urinary leakage, it can be a surgical error, or a result formed as a result of necrosis of the ureter. During our study, we examined the effect of the ureteral suture technique as an independent factor on the development of complications.

It is important to clarify that there were cases where urine leakage and ureteric stricture also occurred during the period under study. Both types of complications typically developed in the early (<30 days) postoperative period. However, ureteral stricture is the dominant type of complication (n=14) in the late postoperative period. An important result is that there is no significant correlation between the suturing technique of the ureteral anastomosis and the development of complications (p=0.184). The rate of urinary tract infections is significantly higher with the UNS technique (p=0.002).

The presence of the BK virus was examined in a small number of cases (n=46). BKV viremia occurred in 55.3% (n = 26) of the examined patients, but none of the cases developed ureteral stricture.

Survival outcomes of complications of ureteral anastomosis

Examining patient and graft cumulative survival using the log-rank test, the presence of UAcomp+ was significantly correlated with graft survival (p=0.010), but was not significant in terms of patient survival (p=0.52).

Results of our study of autosomal dominantly inherited polycystic kidney disease (ADPKD) in kidney transplant recipients

Demographic and clinical outcomes of ADPKD

10.9% (n=80) of the 734 examined recipients were included in the ADPKD group. The age of patients in the ADPKD group (47.5±11.9 years) was significantly higher compared to the non-ADPKD group (40.2±14.1 years) (p<0.001), so patients with this underlying disease are transplanted later, as in the case of other underlying diseases. The rate of urinary tract infection was higher in the ADPKD group (56.0%) than in the non-ADPKD group (44.0%), but the difference was not significant. We examined the presence of extrarenal organ manifestations in the ADPKD group. Polycystic liver in 51 patients (63.8%), confirmed sigmoid diverticulum in 2 cases (2.5%), hiatal hernia in 2 (2.5%), hemangioma hepatis in 1 case (1.3%), adenomatous polyp of the colon in 1 patient (1.3%), gallbladder polyps were discovered in 1 recipient (1.3%) and polycystic horseshoe kidney in 1 case (1.3%). We looked at the prevalence of

comorbidities among ADPKD patients based on literature data. Mitral valve insufficiency occurred in 1 patient (1.3%), aortic valve insufficiency occurred in 1 patient (1.3%), and in 1 case (1.3%) we found brainstem bleeding with a fatal outcome. It is important to emphasize that 90% of patients in the ADPKD group suffer from hypertension (HTN), but de novo HTN did not develop in the remaining 10%. New-onset diabetes mellitus after kidney transplantation (NODAT), as a separate entity, appeared in 6.3% of the ADPKD group we examined, 10% of whom had diabetes already before kidney transplantation.

Test results of removal of polycystic kidneys

We examined the frequency, indications and timing of surgeries for the removal of polycystic kidneys. Before kidney transplantation (KT), nephrectomy was performed in 16 cases, but only 1 case became necessary after transplantation. In 87.5% (n=14) of pre-transplantation nephrectomies, the surgical indication was a high degree of spatial disproportion. In these cases, on the CT findings, the polycystic kidney had visibly reached the iliac fossa area, so the spatial disproportion would have caused a problem during the implantation of the future allograft, which is why these preparatory surgeries became necessary. In 12.5% (n=2) of pre-CT nephrectomies, severe infection and consequent urosepsis were the indication for surgery. The only nephrectomy after transplantation was due to a recurrent, therapy-resistant urinary tract infection. The operation took place 6 months after KT, which meant bilateral nephrectomy.

Acute abdominal surgeries for gastrointestinal perforation in the ADPKD patient group

0.5% (n=4) of the studied population (n=734) underwent acute abdominal surgery due to perforation of the sigmoid colon. Among the patients in the ADPKD group, 1 patient had to be operated on (1.25%) due to perforation of the sigmoid colon. In the case of the non-ADPKD group, 3 patients (kidney transplant due to chronic glomerulonephritis of unidentified origin) underwent acute surgery (0.46%). The result is significant (p=0.007). In terms of immunosuppression, there was no difference, all patients received preparations containing cyclosporin-A (CsA), mycophenolate mofetil (MMF) and steroids (S). Cytomegalovirus (CMV) concordance was always +/+ on the donor (D)/recipient (R) side. One of the patients who underwent acute surgery died.

Survival outcomes in ADPKD

Both cumulative patient and graft survival are slightly worse in the ADPKD group. The 1-, 3-, and 5-year patient survival rates in the ADPKD group were 77.5%, 70.0%, and 62.5% compared to 86.5%, 79.8%, and 73.4% in the non-ADPKD group ($p = 0.013$). Regarding the survival of the implanted kidney allograft, the 1-, 3- and 5-year rates in the ADPKD group were 73.8%, 65.0% and 60.0%, compared to 84.7%, 77.2% and 84.7%, respectively, in the non-ADPKD group. with values of 68.3% ($p=0.008$).

DISCUSSION

The effect of ureteral suture technique on the appearance of complications related to ureteral anastomosis, the effect of reconstruction options on patient and graft survival

The importance of the ureteral suture technique

In our study, among the surgical complications related to ureteral anastomosis, the rate of reoperation was 67.5% (n = 27), which is already comparable with literature data for such a large number of cases. Our own investigation reached similar results to the majority of literature reports, as we found no significant difference between the two types of ureteral suture techniques regarding the effect on the development of complications. In our research, the rate of complications related to ureteral suture requiring intervention was 9.2%, 11.3% for UNS, 7.2% for UU, but the result was not significant. In addition to the number of cases in our center, the rate of complications can be compared with international literature data and can be said to be particularly good. Complications requiring intervention are not related to the technique of ureteral suture at our Clinic, however, in the case of UNS, a significantly ($p=0.002$) higher number of postoperative uroinfections develop.

Use of a double J catheter for ureteral sutures

The protective effect of ureteral stenting can also be seen in the population we studied. At our clinic, the ureteral suture technique of choice is currently the UU, which most centers use or recommend as a secondary option during reoperation. From 1991 to 2013, we usually used epicycstostomy for stenting (at that time, only the UNS was used as the primary ureteral suture), then from 2013 we started using the UU, with the insertion of a DJ catheter in selected cases, and since 2017, according to the protocol. After reviewing our study and literature data, we came to the conclusion that if the recipient has no previous urological intervention, or a dilated ureter or other anatomical complicating factor, then we perform UU and use a DJ stent. In all cases, the accepted practice is the UNS Lich-Gregoir technique or the Röhle-Ziegler technique already proven at our clinic. By choosing the right reconstruction technique during reoperations, patient and graft survival gives good results, which is why it is extremely important for the transplant surgeon to know the various suturing techniques.

At our clinic, since 2020, BKV infections have been systematically screened by PCR testing of blood and urine samples taken in the 3rd, 6th, and 12th months.

Based on our comprehensive Hungarian-language study on surgical complications after kidney transplantation, it can be said that our results are comparable to the data found in the international literature. In Debrecen, the complication rate was as follows: 7.9% of patients had Grade 1, 3% Grade 2, 6.7% Grade 3 and 6.9% Grade 4 complications.

Clinical effects of ADPKD in renal transplantation, timing of polycystic kidney removal

The presence of polycystic kidneys may mean an increased risk for the recipients due to the presence of co-morbidities and a higher frequency of some acute abdominal symptoms. An important task of the transplant surgeon is to determine whether the removal of polycystic kidneys is indicated before the kidney transplant. In some cases, too large own kidneys can cause complications during or after kidney transplantation. It is therefore important to clarify how much attention is given to a significant group, even a tenth of the transplanted population, and according to which professional recommendations we make our decisions. The classic feature of discovering ADPKD is the presence of blood in the urine after physical injury. Two-thirds of these patients had a family history of ADPKD. In most cases, the symptoms appear around the age of forty, which are usually high blood pressure and abdominal pain.

In the patient group we examined, NODAT was detectable in the ADPKD group, HTN was exceptionally high and cardiovascular death proved to be the leading cause of death.

Gastrointestinal acute surgical pathologies

Sigmoid diverticulitis in immunosuppressed patients poses an increased risk for survival. By comparing literature data and our own results, we can state that the disease is more common among recipients with an underlying disease of ADPKD, and pressure symptoms probably related to recurrent infections of ADPKD and resulting from its size are similar to the symptoms of diverticulitis, such as fever, abdominal pain. Given that this group of patients is also used to a milder form of these symptoms and their temporary nature, if the patient does develop diverticulitis, it is possible that they will come to the doctor in an advanced state. It is therefore very important to rule out the possibility of perforation of the large intestine in ADPKD recipients with imaging tests, which in all cases should be an abdominal ultrasound and X-ray examination as the first step. If the patient's kidney function allows it, the specificity of a CT scan with oral contrast material is the highest.

Nephrectomies

In our own practice, we also avoid performing nephrectomies at the time of transplantation due to the increased risk of extended anesthesia time for our recipients with chronic uremia and a significant proportion of them who are older and have heart disease. In ADPKD cases, nephrectomy can be safely performed before transplantation if recurrent UTI, space disproportion, or cancer are suspected. Nephrectomy will not affect graft function. Based on the results, nephrectomy performed in a separate session before kidney transplantation is associated with an overall longer operating time and a higher cumulative risk.

Our study was limited by the retrospective nature of the research, so we were able to determine the presence of certain co-morbidities (e.g. diabetes, high blood pressure) by relying entirely on the patient documentation, assuming that the anamnesis and its documentation fully corresponded to reality. In our study, the presence of the learning curve of new surgeons and the fluctuation of transplant surgeons cannot be detected. For this reason, in addition to the small number of cases, it may happen that some suture techniques and the higher number of complications are temporary. With this in mind, we would like to examine data related to the surgical situation (e.g. night or second surgery), the difficulty of the situation (e.g. multiple arteries), and the transplant surgeon and assistant as possible factors.

SUMMARY

The results of the kidney transplant program in Debrecen are excellent, even in international comparison. At our clinic, the rate of urological complications after surgeries performed between 2010-2013 was 10.4%, while between 2018-2020, this rate decreased to 8%. On average, over the 10-year period, the rate of ureter-related complications requiring intervention was 9.2%, with UNS cases at 11.3% and UU cases at 7.2%. Among these, the rate of ureter (anastomosis) strictures was even lower (8.0% vs. 5.4%), with an average of 6.7%. We did not find any significant difference in the complication rates following the two types of ureteral anastomosis techniques. Complications that developed were successfully managed with urological intervention or, in more severe cases, by re-suturing the ureteral anastomosis. The type of reconstructive procedure did not correlate significantly with the primary ureteral anastomosis technique, meaning that in some patients previously transplanted with UNS, the reconstruction could be UU, or PU/PN, and vice versa. During the reconstructions, only 2 grafts needed to be removed, which represents 0.4% of the entire patient cohort, a very good outcome. The remaining (reconstructed) kidneys are functioning, though their life cycle may be shorter. Based on our results, the development of ureteral complications significantly correlated with the cumulative survival of the grafts, but this only became apparent in the clinic after the second postoperative year. There was no difference in patient survival (89% vs. 87%; $p=0.52$). Recurrent urinary tract infections are a challenge in the kidney transplant population. The rate of urinary tract infections was significantly higher in the UNS technique group compared to the UU group ($p=0.002$).

Among the transplanted patients in Debrecen, 10% were ADPKD patients, and gastrointestinal manifestations were present in 66.3% of the ADPKD group. In 5% of cases ($n=4$), urgent surgery was required due to acute abdomen (colon perforation). In the Debrecen transplant population, NODAT (6.3%) was detected in the ADPKD group, hypertension (HTN) was exceptionally high (90%), and cardiovascular mortality (59%) was the leading cause of death. The removal of polycystic kidneys was mainly performed before kidney transplantation: 16 cases before, and 1 case after the transplant. Preventive nephrectomy not only facilitates transplantation by eliminating spatial imbalance, but also reduces the risk of inflammation arising from the patient's (polycystic) kidney during the postoperative period. The removal of polycystic kidneys should ideally be performed in designated centers, which may not necessarily be the transplanting institution.

NEW SCIENTIFIC RESULTS

1. By examining the results of the Debrecen Kidney Transplantation Program, we were the first in Hungary to analyze and publish the incidence of surgical complications related to kidney transplantation in an international journal, with particular focus on the complications associated with different ureteral anastomosis techniques. Our findings, which are excellent even in international comparison, were used in the development of the Debrecen kidney transplantation clinical protocol.
2. We have determined that knowledge of both the uretero-ureterostomy and uretero-neocystostomy techniques is essential for the success of kidney transplantation at our clinic, and that there is no significant difference in complication rates between the two surgical approaches, both of which are associated with relatively low complication rates.
3. Despite careful procedures, ureteral complications did occur, and for their management, we relied equally (50-50%) on interventional methods and surgical reoperation. The complication resolution rate was notably good, with the direct kidney loss rate being only 0.4%.
4. The use of double J stents during ureteral anastomosis is routinely recommended due to their protective effect. However, compared to our previous practice, the removal of the stents is now suggested earlier (on the 14th postoperative day).
5. After kidney transplants performed at our clinic, we found that the incidence of urinary tract infections was significantly higher in the UNS technique group compared to the UU technique group.
6. The diagnosis of recipients suffering from autosomal dominant polycystic kidney disease requires special attention in the case of abdominal complaints, and the possibility of colon perforation must be excluded.
7. The removal of polycystic kidneys involves a small number of cases, so it is advisable to centralize these surgeries. In cases of disproportion, nephrectomy should be performed before transplantation, and in the case of recurring complaints (urinary tract infection, bleeding), nephrectomy is recommended after transplantation.

ACKNOWLEDGMENT

I owe my gratitude to Dr. Balázs Nemes, who, even as a medical student, sparked my interest in surgery. With his guidance, he supported me throughout my research on kidney transplantation, from my thesis work to presentations at professional congresses, publications, and the writing of my PhD dissertation. By providing continuous new opportunities, he enabled me to remain motivated in my scientific career for over 10 years. His outstanding contribution lies in offering opportunities for young people in the field of scientific work.

I would like to thank Dezső Tóth, who, as the new director of the Department of Surgery, created such a motivating atmosphere that reinforced my belief that sacrifices are worthwhile in the name of science, alongside everyday surgical patient care. As my research neared completion, this further propelled my work.

A prerequisite for my work was that László Asztalos would initiate and then develop the kidney transplantation program in Debrecen, for which I am deeply grateful to him.

I must also highlight, beside Dr. Nemes, Zsolt Kanyári, Roland Fedor, Gergely Zádori, Dávid Kovács, and Péter Nagy, who, as transplant surgeons, contributed significantly to my development through their practical and theoretical advice.

The creation of my dissertation would not have been possible without the assistance of the co-authors of the publications that form its foundation. I would like to particularly thank Réka P. Szabó, Dávid Kovács, Gergely Zádori, Roland Fedor, Zsolt Kanyári, László Asztalos, and Balázs Nemes for their help.

I extend my gratitude to all the staff at the Surgical Clinic of the Clinical Centre of the University of Debrecen who participated and continue to participate in the kidney transplantation program, especially to our head nurse, Tünde Takács, whose experience has been invaluable from the very beginning. I was also able to regularly utilize her practical ideas during my research, as well as the transplant coordinators of the center.

Finally, I would like to thank my wife, Lilla, and my little daughter, Júlia, for their patience and understanding in supporting me throughout this journey.

A certified list of the publications related to the dissertation and list of other publications



**UNIVERSITY of
DEBRECEN**

**UNIVERSITY AND NATIONAL LIBRARY
UNIVERSITY OF DEBRECEN**

H-4002 Egyetem tér 1, Debrecen

Phone: +3652/410-443, email: publikaciok@lib.unideb.hu

Registry number: DEENK/314/2023.PL
Subject: PhD Publication List

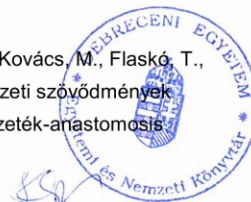
Candidate: Lóránt Illésy
Doctoral School: Doctoral School of Clinical Medicine

List of publications related to the dissertation

1. **Illésy, L.**, Kovács, D. Á., Fedor, R., Zádori, G., Kanyári, Z., Asztalos, L., Nemes, B. Á.: Ureteral Complications Requiring Intervention After Kidney Transplant: A Single-Center Experience. *Transplant. Proc.* 54 (9), 2578-2583, 2022.
DOI: <http://dx.doi.org/10.1016/j.transproceed.2022.10.045>
IF: 1.014 (2021)
2. **Illésy, L.**, Kovács, D. Á., P. Szabó, R., Asztalos, L., Nemes, B. Á.: Autosomal Dominant Polycystic Kidney Disease Transplant Recipients After Kidney Transplantation: a Single-center Experience. *Transplant. Proc.* 49 (7), 1522-1525, 2017.
DOI: <http://dx.doi.org/10.1016/j.transproceed.2017.06.014>
IF: 0.806

List of other publications

3. Legeza, P., Pomozi, E., Tóth, T., Benkő, L., Juhász, G., Kövesi, Z., Veres, É., **Illésy, L.**, Szeberin, Z.: Akut Stanford B típusú aortadissectio konzervatív és invazív terápiájának hosszú távú eredményei Magyarországon. *Orv. hetil.* 163 (16), 637-644, 2022.
DOI: <http://dx.doi.org/10.1556/650.2022.32430>
IF: 0.707 (2021)
4. **Illésy, L.**, Fedor, R., Kovács, D. Á., Kanyári, Z., Zádori, G., Szöllősi, G. J., Kovács, M., Flaskó, T., Tóth, J., Veisz, R., Belán, I., Nemes, B. Á.: Veseátültetés utáni sebészeti szövődmények előfordulása a Clavien-beosztás szerint, különös tekintettel a húgyvezeték-anasztomosis típusára. *Orv. Hetil.* 162 (26), 1038-1051, 2021.
DOI: <http://dx.doi.org/10.1556/650.2021.32278>
IF: 0.707





5. **Illésy, L.**, P. Szabó, R., Kovács, D. Á., Fedor, R., Nemes, B. Á.: Non-Hodgkin Lymphoma in a Kidney Transplant Patient: a Case Report.
Transplant. Proc. 51 (4), 1286-1288, 2019.
DOI: <https://doi.org/10.1016/j.transproceed.2019.04.014>
IF: 0.784
6. Bíró, B., P. Szabó, R., **Illésy, L.**, Balázsfalvi, N., Szóllósi, G. J., Baráth, S., Hevessy, Z., Nemes, B. Á.: Regulatory T Cells in the Context of New-Onset Diabetes After Renal Transplant: a Single-Center Experience.
Transplant. Proc. 51 (4), 1234-1238, 2019.
DOI: <http://dx.doi.org/10.1016/j.transproceed.2019.03.007>
IF: 0.784
7. Nemes, B. Á., P. Szabó, R., Bidiga, L., Kalmár Nagy, K., **Illésy, L.**, Szilvási, A.: Antitestmediált rejkció: kihívás a veseátültetett betegek kezelésében.
Orv. hetil. 159 (46), 1911-1927, 2018.
DOI: <http://dx.doi.org/10.1556/650.2018.31295>
IF: 0.564
8. Bíró, P., Rempert, Á., Mihály, S., **Illésy, L.**, Nemes, B. Á.: Élődonoros vesecseriprogramok Európában. Hol tart Magyarország?
Orv. hetil. 159 (46), 1905-1912, 2018.
DOI: <http://dx.doi.org/10.1556/650.2018.31296>
IF: 0.564
9. Tóth, F., Zádori, G., Fedor, R., **Illésy, L.**, Szabó-Pap, M., Kanyári, Z., Kovács, D. Á., Asztalos, L., Nemes, B. Á.: A Single-center Experience of Allograft Nephrectomies Following Kidney Transplantation.
Transplant. Proc. 48 (7), 2552-2554, 2016.
DOI: <http://dx.doi.org/10.1016/j.transproceed.2016.08.002>
IF: 0.908
10. **Illésy, L.**, Szabó-Pap, M., Tóth, F., Zádori, G., Zsom, L., Asztalos, L., P. Szabó, R., Fedor, R., Nemes, B. Á.: Bacterial Infections After Kidney Transplantation: a Single-Center Experience.
Transplant. Proc. 48 (7), 2540-2543, 2016.
DOI: <http://dx.doi.org/10.1016/j.transproceed.2016.07.011>
IF: 0.908
11. Nemes, B. Á., Fedor, R., Kanyári, Z., Lőcsey, L., Juhász, F., Kovács, D. Á., Zádori, G., Györy, F., P. Szabó, R., Zsom, L., Szabó, T., **Illésy, L.**, Szabó-Pap, M., Kincses, Z., Szabó, L., Damjanovich, L., Balla, J., Asztalos, L.: Eredményeink a teljes jogú Eurotransplant-tagság óta: a Debreceni Vese-transzplantációs Központ tapasztalatai.
Orvosi Hetilap. 157 (24), 925-937, 2016.
DOI: <http://dx.doi.org/10.1556/650.2016.30501>
IF: 0.349





12. Szabó-Pap, M., Zádori, G., Fedor, R., **Illésy, L.**, Tóth, F., Kanyári, Z., Kovács, D. Á., Nemes, B.
Á.: Surgical Complications Following Kidney Transplantations: a Single-Center Study in
Hungary.
Transplant. Proc. 48 (7), 2548-2551, 2016.
DOI: <http://dx.doi.org/10.1016/j.transproceed.2016.07.012>
IF: 0.908

Total IF of journals (all publications): 9,003

Total IF of journals (publications related to the dissertation): 1,82

The Candidate's publication data submitted to the iDEa Tudóstér have been validated by DEENK on
the basis of the Journal Citation Report (Impact Factor) database.

30 June, 2023

