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TRANSPLANTOLOGY

Urological complications after renal transplantation – a single centre experience

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Introduction Urological complications after renal transplantation occur in between 2.5% and 30% of all graft recipients. The aim of the study was to present 7 years of experience in urological treatment of patients with a transplanted kidney. We aimed to identify retrospectively late urological complications in renal transplant recipients at a single center and analyze the treatment modalities and their outcome.

Material and methods Between January 2008 and December 2014, a total of 58 patients after KTX were treated in the Department of Urology because of post-transplant urological complications that occurred during follow-up at the Transplant Outpatient Department. Retrieved data were analysed in retrospectively.

Results In the group of 38 patients with ureteral stenosis (Clavien grade III), 29 patients underwent endoscopy, 8 open surgical procedures and one both endoscopic and open operation. Ten patients were admitted with symptomatic lymphocoele (Clavien III), of which 9 were successfully treated with drainage and one with surgical marsupialization. Because of urolithiasis in the grafted kidney (Clavien grade III), 4 patients were treated with ureterorenoscopic lithotripsy (URSL) and one only with the extracorporeal shock wave lithotripsy (ESWL) procedure. Five urethral strictures plasties and one graftectomy because of purulent pyelonephritis were also conducted. The average age in the group of recipients who experienced urologic complications was similar (46.1 *vs.* 47.8) to those without complications. There was no vesicoureteral reflux or ureteral necrosis requiring surgical intervention, no graft loss and death related to urological complication and treatment.

Conclusions Most complications could be successfully treated with endourological procedures. The kidney function improved in the majority of patients.

Key Words: complications ‹› renal transplantation

INTRODUCTION

Kidney transplantation (KTX) is the optimal treatment for dialysed patients with end-stage chronic kidney disease. It significantly reduces the risk of death (by over 60% compared to dialysis), doubles the expected survival time and greatly improves quality of life [1]. In addition, KTX is cost-efficient compared to dialysis [2].

Many factors influence treatment outcome. Improvements in surgical techniques and upgrades in pharmacotherapy protocols, such as the reduction of steroid dosage and the introduction of multi-drug immunosuppression, have significantly decreased the incidence of surgical/urological complications during the last decades. However, urological complications in renal transplant recipients are still common and their occurrence is associated with significant

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morbidity, impairment of graft function and, in some cases, graft loss and even recipient death.
Urological complications can be divided into early (occurring during first 90 days after the procedure) and late (occurring after 90 days post-procedure).
We aimed to identify retrospectively late urological complications in renal transplant recipients at a single center and analyze the treatment modalities and their outcome.

MATERIAL AND METHODS

Between January 2008 and December 2014, a total of 58 patients after KTX were treated in the Department of Urology as a result of post-transplant urological complications that occurred during follow-up (19–22 months) at the Transplant Outpatient Department. Retrieved data were analysed retrospectively.
A total of 460 kidneys were transplanted between 2008 and 2014 in the Department of Vascular Surgery of Wrocław University Hospital. All kidneys were harvested in the classic manner as per accepted standards concerning the removal of organs of the abdominal cavity. All ureters were anastomosed by the Lich-Gregoire procedure. In the Lich-Gregoire technique, the bladder mucosa is reached via a single cystotomy, and the distal ureter is sutured to the mucosa with an absorbable monofilament 5-0 suture. Subsequently, a tunnel is created to prevent reflux [3]. Routinely, in every recipient a double J (DJ) stent was inserted into the anastomosed ureter during transplantation and was removed after 6 weeks in the majority of cases. The Foley catheter was removed 5–7 days post-procedure. According to standard protocol, patients received 1.5 g cefuroxime once perioperatively as antimicrobial prophylaxis. Suction drains were removed usually at 4 to 5 days after surgery. Patients received calcineurin inhibitors (cyclosporine or tacrolimus), mycophenolate mofetil and steroids as immunosuppressive therapy. In high-risk patients, anti-CD25 antibodies were introduced additionally.
At our centre, the role of the urology department is centered on patient qualification for transplantation, assistance during the procedure in complicated cases and complication management.
Urological complications were diagnosed according to clinical symptoms and kidney function markers, and the use of ultrasound, CT scan, renal scintigraphy and antegrade or retrograde pyeloureterography. All urological complications were categorized according to the Clavien-Dindo classification [4].
The choice of treatment modality depended on the severity of symptoms and complication type.

RESULTS

Between January 2008 and December 2014, of the total of 22 patients after KTX underwent various oncological procedures and 5 were treated due to benign prostatic hyperplasia (BPH) in our Department of Urology. Fifty-eight patients (19 women, 39 men) were treated as a result of post-transplant urological complications. They received their kidney from deceased donors. The mean age in the group of recipients who had experienced urologic complications was similar to those without complications (46.1 *vs.* 47.8 years). The mean donor age was 42.7 years.
Thirty-eight patients (14 females, 24 males) were admitted with ureteral stenosis (Clavien grade III). Diagnosis was confirmed mainly by ultrasound, and in some cases by percutaneous transplant nephrostomy followed by antegrade ureterogram, revealing pyelocaliectasis or ureteropyelocaliectasis. Thirty-five patients had stenosis located at the ureterovesical junction (92.2%). Initially, in 10 patients percutaneous nephrostomy was performed and in 15 patients a double J catheter was reinserted to decompress the collecting system and to ensure the patency of the kidney prior to further treatment. Single endoscopic ureter orifice incision was successfully performed in 29 patients. A total of nine open operations were carried out: in one patient because of a failed endoscopic approach and recurrent stenosis; in a patient with ureteropelvic junction obstruction, a Hynes-Anderson operation was performed; in a case of stenosis in the central ureter, resection of short stenosis and end-to-end anastomosis was carried out; one instance of ureter dissection from massive adhesions; in 2 patients with ureterovesical junction stenosis, reimplantation of the ureter, and 2 Y-V plasties were performed. In all patients a double-J catheter was left in place after the procedure for 6 weeks. Patients' mean kidney function, estimated by GFR, improved from 30 to 48 ml/min after urological treatment.
Ten patients (3 females, 7 males) presented with symptomatic lymphocoele (Clavien grade III). Nine patients were successfully treated with ultrasonography-guided percutaneous drainage performed in the operating theatre. In 6 patients, the procedure was performed only once, whereas three patients required 2–3 drainages, and one, with recurrent lymphocoele (more than 3 drainages), required open surgical drainage with marsupialization.
Five patients (1 female, 4 males) were admitted with stones in the ureters of the transplanted kidneys (Clavien grade III). Three patients underwent single, successful ureterorenoscopic lithotripsy (URSL). Two patients required DJ catheter inser-

tion. One patient had 3 consecutive extracorporeal shock wave lithotripsies (ESWL) performed and expulsed the fragments of stone quickly. The second unerwent 2 ESWL sessions, but these proved unsuccessful; URSL with holmium laser was subsequently performed.
Five patients (1 female, 4 males) with urethral strictures were treated in our department. Three of them had a single successful urethrotomy with optic urethrotome performed. One patient underwent 2 consecutive urethrotomies with a good final result. One patient required open urethroplasty because of longstanding stenosis resulting from iatrogenic injury during catheterization.
There was no vesicoureteral reflux or ureteral necrosis requiring surgical intervention, no graft loss or death related to urological complication and treatment (Table 1).

DISCUSSION

The first successful renal transplantation was carried out on 23 December 1954 by Dr Joseph Murray, a plastic surgeon, and Dr Hartwell Harrison, an urologist [5]. For years, urologists were the primary surgeons to perform renal transplantations. At present, the surgical role of the urologist in renal transplantation has become less important because of, among others, reduced training in vascular surgery for specializing urologists. However, due to specific problems related to the genitourinary tract, urological input in renal transplantation is still vital and the urologist's familiarity with operations on the genitourinary tract is frequently invaluable. Moreover, in many centres urologists perform laparoscopic living donor nephrectomy (LDN). In our urology department, we also perform laparoscopic LDN procedures without postoperative complications. Finally, urological evaluation and intervention is often necessary in patients after KTX to save the transplanted kidney and patient.
Complications such as urine leakage, ureteral stenosis, lymphocoele, lithiasis, urethral stricture and vesicoureteral reflux are reported to occur in between 2.5% and 30% of all recipients, depending on the criteria [6]. The majority of these are ureteral complications arising from anastomosis defects.
The majority of urological complications were managed by endourological approach (82.5%) instead of open surgery. Since 2002, routine insertion of a ureteral stent resulted in a substantial reduction of urinary leakage or fistula. Ureteral stenting, despite lowering the frequency of urinary leaks and early obstruction due to anastomotic edema, can cause urinary tract infections or urethral injury with bleeding. In our centre, the ureteral stent was generally maintained for 6 weeks (but now reduced to 3–4 weeks) and then removed during cystoscopy. Yet, some authors advocate the early removal of the stent at the end of 2 weeks after renal transplantation to decrease the rate of urinary tract infections [7, 8].

Ureteral stenosis

Ureteral stenosis, with urine flow obstruction, was the most frequently observed complication, having occurred in 38 patients. In the literature, ureteral stenosis has been reported as the major long-term urological complication, at a rate of 3–8% [9, 10], but accounted for about 50% of all urological complications. Almost all of our patients (92%) had stenosis located at the ureterovesical junction

Table 1. *Urological complications in kidney transplant patients*

Complication	No. of patients (female/ male)	Mean BMI	Donor gender (f/m)	Mean donor age	Mean recipient age at the time of KTX	Mean time from KTX to treatment (months)	Kidney function (eGFR ml/min/1.73 m²)		Treatment modalities	
							before urological treatment	after urological treatment	Endouro-logical treatment (number of patients)	Open surgery treatment (no. of patients)
Ureteral stenosis	38 (14/24)	27.1	10/28	40.7	44	17.1	30	48	29 endoure-terotomy	9*
Lymphocoele	10 (3/7)	23.1	6/4	46.3	53.8	12.2	54.2	56.7	9 percutane-ous drainage	1 marsupiali-zation
Lithiasis	5 (1/4)	26.7	2/3	45.3	52	75.9	75	76.7	USRL – 4 ESWL – 1	0
Urethral stenosis	5 (1/4)	22.8	4/1	42.5	41.2	9.4	47.3	41	3 urethro-tomy	1 open urethroplasty

KTX – kidney transplantation; USRL – ureterorenoscopic lithotripsy; ESWL- extracorporeal shock wave lithotripsy ; *see ‚Results'

as a consequence of development of fibrosis at anastomosis site. Previous reports indicate that anastomotic stenosis occurred in 60–95% of patients with stenosis. In our department, ureteral stenosis was observed late after transplantion (mean time 17 months). Some authors have described an average time to ureteral stenosis of 5.4 months, but the 10-year risk post-transplantation is estimated to be 9%. Our group observed increased frequency of ureteral stenosis in male patients whose donors were men.

It is believed that ureteral strictures and their subsequent obstructions are caused by surgical errors in anastomosis, ureter ischemia, immunological factors and acute or chronic rejection episodes, infections, and immunosuppressive drugs. It has been proven that dissection of periureteral connective tissue and excessive manipulation of the so-called 'golden triangle' (the site confined by the ureter, kidney and renal artery) should be avoided [9]. These actions can damage the blood vessels supplying the ureter, causing restriction. Necrosis of the distal ureter was reported in up to 70% of patients with damage to this site [11]. Ureteral spatulation length is also an important factor in reducing distal ureteral stenosis incidence. It has been shown that ureteral spatulation of more than 10 mm is effective in decreasing this complication [12]. Another proven risk factor of late ureteral stenosis is Polyomavirus BK (BKV) infection [13].

The therapy of ureteral obstruction must be introduced as early as possible to avoid loss of graft function. A wide range of therapeutic methods is available, depending on stricture location and aetiology. In our department, of the 38 patients with ureteral obstruction, 25 were initially treated with nephrostomy or ureteral stent insertion to restore renal function. Twenty-nine patients with anastomotic stricture underwent single endoscopic ureter orifice incision and double-J stent placement to good effect. The remaining 9 patients (24%) underwent open surgical procedures, including a Hynes-Anderson operation, resection of central ureter stenosis and end-to-end anastomosis, reimplantation of a ureter and 2 Y-V plasties. In patients with multiple or long ureteral stenosis, ureteropyelostomy or ureteroureterostomy can be employed and in cases with an unusable ureter, the 'Boari flap' procedure may be considered [12, 14, 15]

In the majority of the patients, kidney function significantly improved following urological treatment.

Lymphocoele

Lymphocoele occurred in 10 renal transplant recipients. The first-line treatment in every patient with symptomatic lymphocoele was ultrasonography-guided percutaneous drainage without sclerotic agent administration, performed in the operation theatre. Some patients required multiple drainages. One patient with recurrent lymphocoele underwent open drainage with marsupialisation. Percutaneous drainage and fenestration (both open and laparoscopic) are commonly applied in the management of lymphocoele. It has been shown that laparoscopic fenestration is a safe treatment for symptomatic lymphocoele and is associated with the lowest risk of lymphocoele recurrence. Yet, it seems that small and benign lymphocoeles should be treated with percutaneous drainage [16, 17].

The cause of lymphocoele is not entirely clear. It is believed to result from accumulating lymph, originating from lymphatic vessels surrounding the iliac vessels damaged during the operation or from lymph vessels of the transplanted kidney itself. Cautious and limited dissection, with careful ligation of damaged lymphatic vessels, is recommended to decrease the incidence of this complication. It is also important to run proper post-operative drainage.

Urolithiasis

In our department, ureteral calculi were diagnosed in 5 recipients. Transplant urolithiasis occurred 6 years after transplantion. Though the incidence of urinary stones following renal transplantation is low (0.17–1.8%), it is not negligible. Urolithiasis is a dangerous complication due to the risk of obstruction, sepsis, and potential loss of allograft function [18–21]. Symptoms include anuria, renal failure, hematuria and urinary infection. Typical colic pain is rare in patients after KTX because of graft denervation [22]. Urolithiasis following renal transplantation can be both formed de novo or donor-gifted. Factors predisposing to stone formation include amongst others hyperparathyroidism, recurrent urinary tract infection, hypercalciuria, and hypocitraturia [20, 22, 23]

Treatment options for urolithiasis in renal transplant recipients include all methods used in the general population [24]. However, because of altered anatomy and the patient's immunocompromised condition, therapy can be difficult and may be associated with a higher risk of complications. In our department, 4 patients were successfully treated with URSL and 1 patient with 3 consecutive repeated ESWL procedures. Other authors reported less effective treatment of transplant calculi with URSL. On the other hand, Del Pizzo et al. reported a 100% success rate using endoscopic removal of ureteral

calculi. In our study, no complications were observed with the above-mentioned procedures.

Urethral strictures

In addition to the above, 5 patients with urethral strictures were treated in our department. The successful urethrotomy with optic urethrotome was performed in 4 patients, with the remaining patient requiring open urethroplasty because of long-standing stenosis, resulting from iatrogenic injury during catheterization. Urethral strictures following KTX are rare, yet serious complications, possibly leading to hydronephrosis and graft function deterioration. Urethrography is very useful in revealing the precise location and length of the urethral stenosis. Urethral strictures may be associated with iatrogenic urethral injury, prolonged catheterization time and urinary tract infection. Therapeutic options include urethral dilation, endoscopic urethrotomy or urethra reconstruction [25].

The urological treatment was successful in all patients: renal transplant function improved, with neither graft loss nor patient death. Over the last decade, the ratio of endoscopic to open surgical procedures in the treatment of urological complications has more than doubled, with about 76% of complications treated endoscopically. In our previously published paper concerning the period 1983–1999, we reported a rate of only 43% [26].

CONCLUSIONS

The improvement of transplant surgery techniques has subsequently decreased the incidence of severe urological complications in renal transplant recipients. Most of these complications can now be successfully treated with endourological procedures. Open surgical procedures were employed mainly in patients with severe ureteral strictures. Kidney function improved in the patients being treated and there was no graft loss.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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