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PREVENTION AND SURGICAL TREATMENT OF UROLOGICAL COMPLICATIONS IN KIDNEY TRANSPLANT RECIPIENTS

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Post-kidney transplant urological complications (failure of a newly formed anastomosis, obstructive uropathy, necrosis of graft ureter, graft ureteral stricture, development of vesicoureteral reflux in the renal graft, recurrent urinary infection) are one of the main causes of graft loss and various deaths. This literature review aims at analyzing world studies on prevention methods (routine graft ureteric stenting) and surgical techniques for treating urological complications (laparoscopic correction of supravesical urinary tract obstruction in a graft kidney) in kidney recipients.

Keywords: urological complications, kidney transplantation.

With all significant achievements and progress in treating kidney recipients, urological complications remain the main causes of long hospital stay, graft loss, and death of recipients in the earlier and later postoperation stages [1–2]. The main urological complications developing in kidney recipients are failure of the newly anastomosis (1.5–6%), obstructive uropathy (0.9–7.5%), necrosis of the graft ureter, stricture of the graft ureter (3.0–12.6%), development of vesicoureteral reflux in the renal graft (5.0–20%), and recurrent urinary tract infection. The latter is one of the biggest problems for patients on the prolonged immunosuppressive treatment and one of the leading mortality causes after kidney transplantation reaching 5 to 10% in the 1st year [2–5]. Most often, urological complications occur during the first two weeks after transplantation and are manifested by a decrease in urine output and impaired graft function [6]. The results of the treatment of urological complications in kidney recipients are associated with the time of the diagnosis. So far, the question remains open of the methods of surgical interventions indicated in the prevention and treatment of urological complications.

The urological complications rate after kidney transplantation in early studies (1970–1990) varied from 4.2 to 14.1% [7], in later studies (1990–2000) it was 3.7–6.0% [8], while at present they rate from 2 to 5% [9], which is probably reflecting of various stages of the development of transplantation, the improvement of diagnostic methods and the advance of surgical skill.

In their retrospective study, M. Whang et al. analyzed the results of 2,548 kidney transplantations and detailed the following urological complications (5.5%): reflux in the renal graft (3%), strictures of the graft ureter (1.3%), uroplania (0.9%), and urinary obstruction (0.3%). Among the factors affecting the reduction in the number of urological complications, there were single surgeon manipulations, the use of a shorter segment of the ureter by Lich-Gregoire (compared to Politano-Leadbetter) method, and routine ureter stenting [9]. The following independent risk factors for the development of the urological complications were identified: male donors, male recipients, African American recipients, Taguchi method, graft artery reconstruction, multiple renal arteries, and diabetes in recipients [10–11].

Failure of the newly anastomosis. The uroplania prevalence after kidney transplantation, which can occur shortly after transplantation or in the later postoperative period, is 1.5 to 6%, [4; 12]. In most cases, the uroplania occurs in the anastomosis area, at the bladder, ureter or kidney pelvis levels [6].

At the formation of pyeloureteral anastomosis, uroplania can occur due to improper installation of the proximal stent helix or the pelvis perforation at its installation [6; 13]; also, the uroplania may be caused by the atrophied bladder mucosa and dysfunction of the urethral catheter against the background of polyuria with the early (up to 6 weeks) removal of the urethral catheter [14].

In the first hours after surgery, the uroplania is most often manifested by an increase in the drainage volume, profuse wound blotting and delayed graft function. Most commonly, the biochemical analysis of drained fluid shows high creatinine, urea and Ca levels [15]. The indirect signs of uroplania are the concretion over the graft, genitals or thighs swelling, fever, urine output decrea-

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sed to anuria, and increased plasma creatinine [15]. The uroplania occurring in one to two weeks after surgery is caused by the ureter necrosis due to insufficient blood supply (the distal ureter is most at risk during the graft treatment) [15–16]. The delayed uroplania diagnosis can lead to inflammatory processes (abscess) in the area of the transplanted kidney and the generalized infectious process in the patient [14].

It was shown that the uroplania is less common in patients with the ureter anastomosis with the ureter stent [13].

Obstructions. These are the most diverse group of complications; they pose a serious risk of loss of transplanted kidney function and are observed in 0.9–7.5% of recipients [3]. According to J. Aurio, the incidence of obstructive uropathy is 3–4%, and the risk of their development is higher in recipients with a kidney from a donor over 65 with a graft with more than two arteries [17].

Obstructions directly related to the anastomosis formation. Ureterocysto- (pyelouretero-, ureteroanastomosis) obstruction at the sutures area, the ureter compression in the submucosal tunnel, the ureter torsion or inflection (positional obstruction).

An insufficient length of the ureter leads to an increase in the mechanical load on the anastomosis and causes a urinary fistula, while its excessive length leads to the ureter torsion and violation of the urine outflow [9]. A radical way to correct the recurrent complications is to form the pyeloureteroanastomosis with the recipient's ureter. In case of ureterocystoanastomosis obstruction (including the ureter compression in the submucosal tunnel), at the ureter torsion or inflection, the reimplantation of the ureter into the bladder is recommended [2].

Compression obstructions. The compression obstructions relate to the graft ureter compression from outside by a lymph cyst, testicular cord, abscess, neoplasm, urinoma, and hematoma.

The recurrent obstructive complications of the immediate postoperative period (to 12 weeks) include the ureter compression by a lymph cyst (found in 0.6–51% of kidney recipients) [6]. The formation of a lymph cyst is tied to an insufficiently thorough ligation of the lymphatic ducts at the identification of main blood vessels and graft treatment [18]. An increase in lymph secretion is provoked by a violation of the venous outflow, rejection episodes, and even mechanical injury to the kidney. A rational way to eliminate a lymph cyst is its marsupialization or internal drainage into the abdominal cavity, provided there is no lymph cyst pyosis [19]. In the immediate postoperative period, an external ureter compression usually develops no earlier than by the second postoperation week and can be caused by a large hematoma, urinoma, and even an abscess. Further on, the presence of a hematoma sometimes leads to the development of retroperitoneal fibrosis and ureter stenosis that usually occur in several months after kidney transplantation [13–14].

Obstruction of the ureter interior lumen. It can be obstructed by blood clots, necrotic masses, concrements, foreign bodies, and neoplasms.

The ureter necrosis is one of the adverse complications in the immediate postoperative period [20]. An excessive excision of periurethral tissue and the use of the ureter of excessive length are common causes of the ureter necrosis [16]. The correction method depends on the extent of the alterations. First, a puncture nephrostomy is performed to adequately drain the kidney collector. At maintained ureter patency, its antegrade stenting is possible [3]. At complete obliteration of the ureter, the formation of anastomosis of the graft pelvis with the recipient ureter is proposed.

The ureter obstruction by concrements is detected by the routine ultrasound examination. Due to complete graft denervation, the renal colics are absent, though a sensation of heaviness and fullness in the iliac region may be present (due to pressure on the surrounding tissues), urethrodynia, fever, arterial hypertension, urine amount decrease up to anuria (at complete obstruction) [9]. With even a moderate expansion of the pyelocaliceal system of the graft in recipients, the antegrade pyeloureterography is indicated [21].

Sclerotic obstructions. The later period is mostly featured by obstructive complications due to the development of ischemic ureter stricture, retroperitoneal fibrosis or the bladder wall sclerosis and, though much less commonly, of the ureter occlusion by calculus.

The reflux in the renal graft occurs in 1–50% of recipients, despite the use of the antireflux technique for the anastomosis [formation 3; 16; 22]. According to the literature, there is no negative reflux effect on the function of the transplanted kidney. This can be explained by the fact that the graft ureter is denervated and its length is small; therefore, when the active reflux occurs, the high hydrostatic pressure in the kidney collector, which is the damaging trigger, persists for a short time and then rapidly drops [23]. Thus, functional (and especially organic) changes in the renal graft have no time to develop. In their study, M. Margreiter et al. found that reflux does not affect such long-term outcomes as the graft survival, the recipient, the incidence of urinary tract infections, and the proteinuria severity [24].

The reflux in the renal graft is divided into active (at urination), passive (at the bladder filling), and mixed [25].

The question of the need for reflux correction is related to the degree of its influence on the graft function. An indication for surgery is the persistent vesicoureteral reflux, leading to impaired renal graft function. The remedial procedure may fail at insufficient volume and rigidity of the bladder wall, which is often in patients with chronic kidney disease after prolonged anuria. In the

presence of their own unaltered ureters, the most radical way to eliminate massive reflux in the graft is the end-to-end pyeloureteroanastomosis [9]. However, according to some surgeons, the surgery of the reflux in the renal graft could be resorted to the most extreme cases when graft function cannot be preserved by other methods. In this, less traumatic endourological transurethral correction methods are more commonly used.

The vesicoureteral anastomosis stricture is the most common urological complication after kidney transplantation. The rate of ureter stricture in kidney recipients, according to various sources, ranges from 0.9 to 34% [7; 9; 19–20; 26].

The ureter strictures are usually classified as early (<3 months) and late (>3 months) after kidney transplantation. The early ureter strictures can be caused by foldings, temporary swellings of the ureter wall, narrow anastomosis or external compression, hematoma or lymph cyst [5; 19]. The late ureter strictures are usually associated with poor ureter vascularization, leading to ischemia and the development of retroperitoneal fibrosis. The following risk factors were identified: the donor age over 65, prolonged cold ischemia, the presence of several renal arteries, delayed graft function, and a vesicoureteral anastomosis without a stent [20]. Another cause of the late ureter stenosis (2–6% of all cases) is RSV infection (poliomaviruses). Histologically, the stenotic region of the ureter looks ischemic and fibrous [26].

In a retrospective study of S. Buresley, the outcomes for 646 kidney grafts from live relative (n = 461) and deceased (n = 185) donors to patients, 81 of which were children, were analyzed. The ureter strictures (n = 15, 2.58%) were diagnosed in the later period after transplantation and was more common among children (4.23%), uroplania was observed in the early postoperative period and was more common in elderly (4.69%) patients [8].

Routine ureter stenting in patients at kidney transplantation. A lot of modern studies are aimed at assessing the role of routine ureter stenting in the development of urological complications in kidney graft recipients [27–31].

M.R. Laftavi found that the vast majority (97%) of kidney recipients without signs of bladder dysfunction who received standard kidneys without signs of ureter blood supply violation can be successfully operated without the routine use of stents [32]. It has been shown that the rate of urological complications is higher after transplantation of a kidney from a living donor, while the incidence of urinary tract infections is higher after kidney transplantation from deceased donors [33].

The routine use of stents for kidney transplantation can lead to such problems as migrated, encrusted, broken and forgotten stents, as well as pain in the lower urinary tract, hematuria and dysuria due to the small volume of the bladder [34].

Many authors state that the routine use of ureter stents favors the development of urinary tract infections, which can lead to transplanted kidney dysfunction and even death [35–37]. J. Gozdowska et al. attributed the installation of the ureter stent to risk factors for infectious complications at kidney transplantation (more often in males) (n = 34; 32%, p = 0.021) [36].

However, some studies have not found a significant difference in the incidence of urinary tract infections in kidney recipients with and without routine ureter stenting [38–41].

To solve the matter of UTI on the background of immunosuppressants in kidney recipients with stented ureters, the early stent removal is proposed [31; 37; 42–43]. Various transplantation centers report different optimal stent removal times after transplantation, ranging from 5 days to 6 weeks [41; 43–44].

Based on an analysis of kidney graft outcomes with routine ureter stenting in 48 patients, A.K. Coskun showed that early stent removal at the end of the 2nd week after kidney transplantation reduces the incidence of urinary tract infections by 2% vs. 35% (at stenting for over 2 weeks). Urological complications were not detected in any group [44]. P. Patel showed that the UTI rate was 24.6% with the stent removed after 6 weeks and 7.6% when removed on day 5 after kidney transplantation [43].

The updated Cochrane meta-analysis, which included seven randomized controlled trials, recommended the routine use of stents during kidney transplantation due to the low incidence of uroplania (1.02% vs. 5.28%; 95% CI [0.12–0.74]) and obstruction (0.51% vs. 4.40%; 95% CI [0.09–0.81]) in the group with stents [28]. However, the routine ureter stenting has been shown to increase the incidence of urinary tract infections (26.3% with a stent vs. 17.9% without a stent; OR = 1.49; 95% CI [1.04–2.14]; p = 0.03); when the stent stays for over 6 weeks, there is a risk of the stent encrusted with urinary salts [28].

A. Tavakoli et al. found that the routine use of the ureter stent at kidney transplantation reduces the risk of uroplania and urinary obstruction, while the incidence of urinary tract infections increases significantly when the stent stays longer than 30 days (p < 0.01) [29].

An intermediate analysis of a randomized prospective double-blind study showed that the ureter stent removal in 1 week reduces the UTI risk compared to the routine removal in 4 weeks (OR = 8.791; 95% CI [1.984–38.943]; p = 0.004) [45].

In their meta-analysis, J.F. Cai et al. found that early (≤7 days) removal of the ureter stents after kidney transplantation did not significantly increase the frequency of postoperative urological complications (ureter stricture, ureter obstruction, and uroplania) compared to late (≥14 days) removal (OR = 1.87, 95% CI [0.45–7.70], p > 0.05). A significant difference was observed in the UTI incidence between the early and late removal groups

with ureter stents (OR = 0.43, 95% CI [0.32–0.59], p < 0.01) [46].

Despite the high UTI risks, the current data suggest the routine use of stenting. Determining the optimal time for the ureter stents removal is important to minimize the risk of such complications as urinary tract infections associated with prolonged exposure and to prevent urological complications in patients after kidney transplantation.

Treatment of ureter strictures of a transplanted kidney. Balloon dilatation and temporary stenting of the ureter are the most common endourological procedures. As a rule, the percutaneous drainage of the pyelocaliceal graft is considered the first option, since it is simpler and has both diagnostic and therapeutic implications at hydronephrosis [47]. In the short term, endourological procedures have a high measure of efficacy (73 to 100%), which in the long term decreases to 40–55% due to the high relapse rate [48]. There are reports on the success rate of minimally invasive treatment of ureter strictures ranging from 49% to 100%, depending on the extent, stricture location, and the treatment method [47–48]. Helfand with colleagues reported on the experience of surgical treatment of ureter strictures after kidney transplantation and proposed a stricture treatment algorithm based on the stricture size (<3 cm) and the time between transplantation and epy stricture diagnosis (<3 months) [49]. In a review by Haberal et al., the recurrent balloon dilatation is recommended for resistant strictures, whereas for fibrous strictures, the temporary post-dilatation stenting is suggested. They tried to determine a treatment strategy for kidney recipients who develop ureter strictures [50]. In B. He et al., three classes of ureter strictures were determined: the 1st included hydronephrosis with ureter stenosis without strictures, the 2nd – hydronephrosis with a stricture of ≤1 cm, and the 3rd – hydronephrosis with a stricture of more than 1 cm [51].

The balloon dilatation of ureter strictures has become one of the first correction methods for patients with transplanted kidneys and showed its efficacy of 51% (44–62%) with a follow-up period of 17 to 78 months [52]. The balloon dilatation has proven effective in the treatment of ureter anastomosis with obstructive megaureter and with ureter strictures of 1 cm or less in kidney recipients [53].

In Ooms LSS retrospective study, the antegrade balloon dilatation was shown to be an effective treatment for ureter strictures after kidney transplantation, since it is minimally invasive and can prevent surgical treatment of strictures in almost 50% of cases [54].

M. Balaban et al. evaluated the efficacy of minimally invasive treatment of ureter strictures by retrograde stenting of the ureter of a transplanted kidney. Ureter strictures were found in 13 patients (1.26%) out of 1,026. The overall success rate of the introduction of a retrograde ureter stent on the first try was 75%, and the success of replacing the stent was 100%. The renal function remained stable in all patients for 41 months; no complications were detected. Thus, the method of retrograde stenting of the ureter with strictures is safe and effective in kidney recipients who are not indicated for open surgical reconstruction [55].

E.G. Yushina et al. established the benefits of preventing the failure and strictures of ureterocystoanastomosis of a transplanted kidney and of the endoscopic methods for correcting urological complications after a kidney transplantation [56].

The higher efficacy was observed with simultaneous dilatation of stricture and electro incision of the ureter wall, which is feasible with a destructor. During the follow-up period (19 months), the efficacy of the method for localization of ureter strictures in the distal region increased to 78% (60 to 100%) [21; 52].

Despite the increased potential for percutaneous obstruction correction, there remains a certain category of patients requiring surgical treatment. Surgery is indicated at the complete obliteration of the ureter in a significant area or when it is technically impossible to percutaneously remove the obstruction to the urine outflow. In some patients, using endoscopic methods and open surgery, it is not possible to restore an adequate urine passage from the graft.

J. Kwong et al. note that at the violation of the urine outflow from the graft, the most common minimally invasive correction method is the endourologic treatment, providing a successful outcome of up to 58.6% (95% CI 50.1–66.7, n = 133) [57], and up to 81% with open surgical correction methods [57–58]. The majority of the current studies show a similar rate of urological complications in the groups with ureteroneocystoanastomosis and ureteroureteroanastomosis / pyeloureteroanastomosis [59].

The balloon dilatation and laser pyelo- or ureterotomy have good clinical outcomes in patients with strictures of no more than 2 cm. If a stricture recurs, repeated dilatation and laser pyelo- or ureterotomy are not recommended [60].

D.A. Perlin et al. demonstrated the possibility to perform pyeloureteroanastomosis using the recipient's ureter (n = 2) in the treatment of urological complications after kidney transplantation with the laparoscopic method [61].

CONCLUSIONS

The review and analysis of literature data on the prevention and surgical correction of urological complications in transplanted kidney recipients make it possible to conclude that the problem is currently being comprehensively studied all over the world.

In patients after kidney transplantation, there is a risk of urological complications due to prolonged anuria before surgery, a small bladder volume, ischemia, necrosis, stenosis or compression of the graft ureter; therefore,

despite the risk of developing infectious complications, the issue of routine stenting of the graft ureter and the timing of its removal still appear relevant for the prevention of urological complications.

Analyzing the literature, we found some unresolved issues in the tactics of surgical treatment of post-transplant urological complications arising in kidney recipients in the long term. Traditionally, the correction of urological complications has been performed by open surgery, which, in turn, was a traumatic procedure for the patient, with a complicated postoperative period and slow healing of postoperative wounds against the background of immunosuppressive therapy. Currently, what comes to the fore is the implementation of minimally invasive surgical methods that reduce the risk of postoperative complications, diminish indications for open surgical interventions, and shorten the hospital stay; however, we still lack the precise and complete protocols and algorithms to treat urological complications after kidney transplantation.

The authors declare no conflict of interest.

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