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Nephrolithiasis in related kidney donors

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Abstract

Introduction. Long-term results of renal transplantation from living donors are much better than the results of cadaveric transplantations. Recently, because of the shortage of living donors, some centers have started using kidneys from living donors with asymptomatic stones as a potential solution for the problem. However, the optimal surgical solution for such situations has not yet been developed.

Aim. To evaluate our obtained transplantation results of using the kidneys from living donors with nephrolithiasis and compare them with the literature data.

Material and methods. In the period from 2012-2021, renal transplantations in our clinic were done in three patients from related donors with stones in the kidney. One donor underwent minipercutaneous lithotripsy one month prior to nephrectomy. The other two underwent simultaneous retrograde lithotripsy and laparoscopic donor

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nephrectomy. In these cases a holmium or thulium laser was used for the destruction of calculi. All donors underwent laparoscopic retroperitoneal nephrectomy.

Results. All stones were successfully removed. There were no surgical complications in donors during and after procedures. Warm ischemia time did not exceed 3.5 minutes. The general length of hospital stay was 10 days in case of predonation stone removal surgery and 6 and 4 days in the cases of simultaneous procedures, respectively.

All grafts were transplanted to related recipients. One of the recipients was treated with hemodialysis before transplantation, the other one with peritoneal dialysis. The third recipient underwent preemptive transplantation (before the start of dialysis). The graft function in all cases was immediate. During the follow-up period (9-57 months), no signs of nephrolithiasis were seen in either donors, or recipients.

Conclusions. Consideration of potential donors with stones in one kidney might increase the number of living donor renal transplantation. Simultaneous RIRS and laparoscopic donor nephrectomy can be considered as an alternative to sequential operations or ex vivo stone extraction. The presented technique is reproducible, safe and was not associated with an increased length of hospital stay.

Keywords: nephrolithiasis, kidney transplantation, laparoscopic donor nephrectomy

Conflict of interests Authors declare no conflict of interest

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BMI, Body Mass Index
ESWL, extracorporeal shock wave lithotripsy
GFR, glomerular filtration rate
HL, holmium laser
HLA, human leukocyte antigen
PNLT, percutaneous nephrolithotripsy
P-U, pyeloureteroanastomosis
RIRS, retrograde intrarenal surgery
TL, thulium laser
U-C, ureterocystoanastomosis

Introduction

Long-term results of kidney transplantation from living donors are significantly better than those from post-mortem donors. However, in recent years there has been a downward trend in the share of such operations. In addition, living related donor transplant operations significantly expand the possibility of performing preemptive transplantations in patients with end-stage chronic renal disease, being elective surgery, in contrast to kidney transplantation from post-mortem donors, when the timing of surgery is not predictable [1–5]. An ideal kidney donor should be free of kidney disease, vector-borne infections, and malignancy. However, with an increase in the total number of transplantations, the share of operations from living donors in many centers has gradually been decreasing [2].

The situation can be improved, among other things, by attracting potential donors with expanded criteria. The use of living donors having solitary stones in the kidney has increased the number of transplantations in some clinics [6]. Traditionally, the presence of stones in the upper urinary tract has been considered a relative contraindication to kidney donation, as they can cause infection, hematuria, and even urinary tract obstruction in the recipient [7, 8].

Removal of an intact kidney runs counter the basic principles of lifelong donation and creates a risk of complications for the donor in the long term. In principle, the donor may be at risk of stones even in the remaining "healthy" kidney in the future, which can also lead to infection, obstruction, and eventually even kidney failure [9]. However, recently, kidneys with solitary asymptomatic stones have been recognized by some centers as suitable for donation in selected cases [10-12]. Persistent organ shortage and the development of minimally invasive interventions have stimulated research aimed at removing stones before kidney donation and even ex vivo immediately before transplantation [10]. In some clinics, the recruitment of donors with urinary tract stones has led to an increase in the number of transplants by about 5% [13]. However, the optimal way of surgical solution for such situations has not yet been developed. The question of the expediency of preliminary removal of calculi from the donor, or their extraction ex vivo (bench surgery) just before transplantation has still remained the subject of discussion. The aim of our study was to assess our own results of using a kidney from living donors with nephrolithiasis for transplantation and make comparison with the literature data.

Material and methods

During 2012-2021, in the Volgograd Regional Uronephrological Center, kidney transplantations were performed in three patients from living related donor with calculi in one kidney. Two more potential donors were rejected due to the presence of a small calculus in the opposite kidney and a history of repeated renal colic. All other potential donors had asymptomatic nephrolithiasis. Additional selection criteria for potential donors were the total glomerular filtration rate of at least 85 ml/min*1.73 m², no hyperuricemia, hypercalciuria, hyperoxaluria. Examination of potential donors, including computed tomography or magnetic resonance imaging (Fig. 1), was performed after obtaining a negative lymphocytotoxic test (cross-match). The acceptable contribution of the remaining kidney - according to radioisotope nephroscintigraphy - was considered to be at least 50%. All donor-recipient pairs matched in AB0 blood type, mismatch in human leukocyte antigens (HLA) were 3, 3, and 4, respectively.

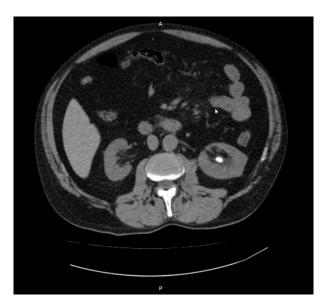


Fig. 1. Computed tomogram of the potential donor. Native phase. Stone in the medial calyx of the left kidney

One donor had previously undergone mini-percutaneous nephrolithotripsy one month prior to nephrectomy. The other two underwent simultaneous retrograde nephrolithotripsy and laparoscopic donor nephrectomy (Table 1). The calculus destruction was performed by using a holmium laser in two cases, a thulium laser in one case. All donors underwent laparoscopic retroperitoneal nephrectomy according to the clinic's originally modified technique. In one of the donors, an ureteropelvic segment stricture was additionally found

Donor	Stone size, mm	Stone location	Calculus density, HU	Access for stone elimination	Duration of lithotripsy, min	Type of energy	Lithotripsy mode	Hospital length of stay, days
1	10	pelvis	1326	Mini-PNLT	10	HL	6.0 Hz 1.00 J	4+6
2	7	medial calyx	987	RIRS	35	TL	60.0 Hz 0.10 J	6
3	5 and 8	bottom calyx	1171	RIRS	40	HL	20.0 Hz 0.20 J	4

 Table 1. Basic parameters for performing nephrolithotripsy

Notes: HL, holmium laser; HU, Hounsfield units; TL, thulium laser, mini-PNLT, mini-percutaneous nephrolithotripsy; RIRS, retrograde intrarenal surgery

The technique of simultaneous retrograde nephrolithotripsy and laparoscopic donor nephrectomy

Preliminary stenting was not used in order to reduce the period of disability and avoid additional procedures for the donor. Under combined anesthesia, the donor was placed on the operating table in a lithotomy position. After visualizing both orifices, a guidewire, plastic bougie, and a protective casing were successively inserted into the ureter from the side of interest under the control of the C-arm imaging unit. Further, a flexible ureterorenoscope was passed along, to the pelvis. In both cases, a disposable ureterorenoscope Lithoview (Boston Scientific, USA) was used in order to minimize the risk of infectious complications in the recipient while on immunosuppression. After visualization of the calculus, its laser destruction was performed in the energy mode of 0.1-0.2 J/20-60 Hz using a 270 µm light guide (Fig. 2). After visual

inspection of possible residual fragments and damage to the mucosa, the instruments were removed.

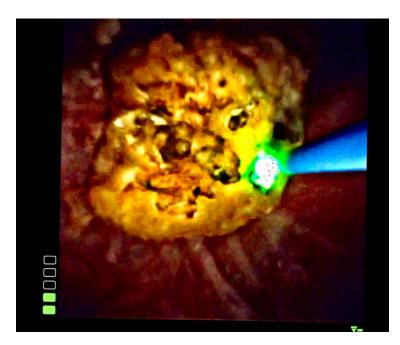


Fig. 2. Kidney donor. Retrograde laser nephrolithotripsy

The donor was placed to the position on the opposite side at an angle of 90°, and the table surfaces were positioned with extension in the lumbar region. Access under the external f. endoabdominalis layer was obtained through a 1.5 cm incision along the posterior axillary line at 1 cm below the 12th rib. The working space was formed using a latex balloon. Using Janet syringe, 600–800 ml of air was injected into the balloon. After a 2-3-minute exposure under a finger control, a 10-mm port was placed in the mid-axillary line at 1.5-2 cm above the iliac crest, and a 12-mm port was placed in the primary access area. Then, after the formation of carboxyrethroperitoneum (12–14 mm Hg), a 5-mm port was placed under a camera control along the anterior axillary line under the costal arch.

First of all, the lumbar muscle was visualized. Moving medially along the psoas muscle, after dissection of Gerota's fascia, the aorta was visualized on the left, as well as the lumbar vein, which was transected with LigaSure. After that, the renal artery was released circularly. The gonadal and adrenal veins were sequentially transected using LigaSure, then the renal vein was loosened (Fig. 3). After isolating the vessels, the posterior surface of the kidney, the upper pole made separated from the adrenal gland, the anterior surface were sequentially released from the surrounding fatty tissue. Last, the lower pole and ureter were isolated in combination with the surrounding tissue and the gonadal vein. After crossing the distal end of the gonadal vein and the ureter, the kidney was also "tilted" backwards using LigaSure, making sure that it was completely exposed and fixed only by the vessels (Fig. 4).

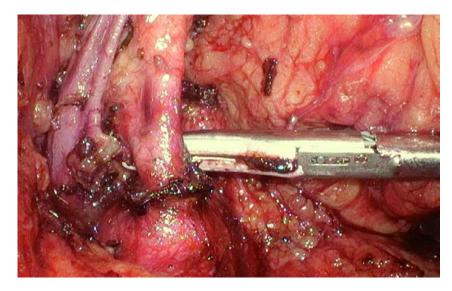


Fig. 3. Simultaneous retroperitoneoscopic donor nephrectomy on the left side. Mobilization of the renal vessels

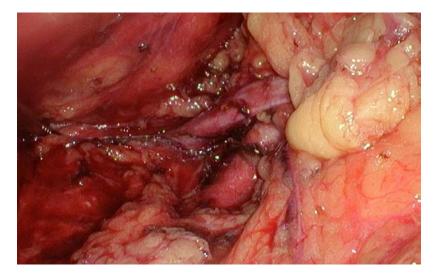


Fig. 4. Simultaneous retroperitoneoscopic left-sided donor nephrectomy. Control of renal mobilization: anterior surface

In order to improve the cosmetic effect, we formed an extraperitoneal tunnel to the suprapubic region (Fig. 5). After that, a transverse suprapubic incision (6–7 cm) was made in the skin, subcutaneous tissue, anterior layer of the rectus abdominis muscle sheath, without spreading the muscles to preserve carboxyretroperitoneum.

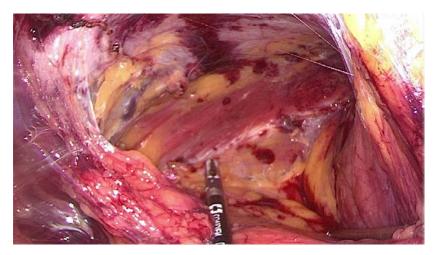


Fig. 5. Simultaneous retroperitoneoscopic left-sided donor nephrectomy. Extraperitoneal tunnel formation

After partial immersion of the fully mobilized kidney into the container, the renal artery was clipped twice and transected, and then the renal vein was transected. The rectus abdominis muscles were spread apart and the container with the organ was removed.

The kidney was perfused with cold Custodiol solution supplemented with 5000 IU of heparin. The ex vivo graft preparation was carried out in a solution with melting ice at 4°C.

Kidney transplantation was performed according to the standard technique into the iliac region, using the internal or external iliac artery and external iliac vein for anastomoses. The ureterovesical anastomosis was formed on the internal stent according to the Barry technique. In case of pyeloureteral segment stenosis, the graft pelvis was anastomosed endto-end with the recipient's ureter, also on a stent (Fig. 6).

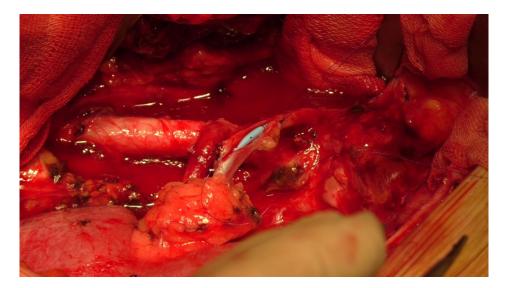


Fig. 6. Allotransplantation of the kidney from a related donor. Formation of pyeloureteroanastomosis

Postoperative follow-up of patients included standard monitoring of biochemical parameters with calculation of glomerular filtration rate (GFR), ultrasound examinations. Recipients underwent additional testing for the most common viral infections and monitored for blood levels of immunosuppressants.

Results

Calculi were successfully removed from all donors. The type of laser used made no difference for the procedure duration (Table 1). No surgical complications occurred in any donor at either the lithotripsy stage, or the subsequent stage of kidney removal. All nephrectomies were performed laparoscopically without conversion. The main perioperative parameters are given in Table. 2. The period of warm ischemia did not exceed 3.5 minutes. The blood loss volume was 80, 50 and 100 ml, respectively. No visible damage to the grafts during extracorporeal handling was found. In case when the removed left kidney had two renal arteries, the inferior pole artery was anastomosed end-to-side with the main one. With preliminary removal of the calculus, the total hospital length of stay for a donor was 10 days; with simultaneous nephrolithotripsy and nephrectomy, the hospital length of stay was 6 and 4 days, respectively.

Donor	Gender/ age	BMI, kg/m ²	Side of nephrectomy	GFR before surgery, ml/min* 1.73m ²	Contribution of the removed kidney, %	Time interval between lithotripsy and donor nephrectomy	Nephrectomy duration, min	Warm ischemia time, min	Follow-up period, months
								a a	= 0
1	f/40	30.5	right	112	38.7	1 month	135	2.3	58
1 2	f/40 f/51	30.5 34.1	right left	112 95	38.7 45.3	1 month simultaneously	135 125	2.3	58 26

Table 2. Key perioperative data on donor nephrectomies

Notes: BMI, body mass index, GFR, glomerular filtration rate

All kidney transplants were performed to related recipients. One of the recipients received hemodialysis replacement therapy before transplantation, other one received peritoneal dialysis. The third recipient underwent preemptive (pre-dialysis) transplantation. No surgical complications were seen during kidney transplantation or in the immediate postoperative period. The graft function in all cases was immediate. The hematuria in all recipients was insignificant, short-term and did not differ from that typical for a standard kidney transplant. Retroperitoneal drains in recipients were removed 24–52 hours after surgery, internal stents were removed on days 19–21. During the followup period (9–57 months), there were no signs of nephrolithiasis in donors or recipients, and the graft function remained stable in all the cases (Table 3).

Recipient	Gender/age	Relation to the donor	HLA mismatches with the donor	Method of urinary tract reconstruction	Surgery duration, min	Plasma creatinine before transplantation, µmol/L	Plasma creatinine at discharge from hospital, µmol/L	Hospital length of stay, days	Follow-up period months
1	m/29	Brother	4	U-C	155	825	138	28	57
2	w/22	Daughter	3	U-C	145	567	122	25	26
3	m/18	Son	3	P-U	125	1150	89.1	22	9

Table 3. Key data of renal transplant recipients

Notes: U-C, ureterocystoanastomosis; P-U, pyeloureteroanastomosis

Discussion

Strict selection of living donors has a decisive influence on the success of transplantation. With the growing demand for transplantation, many centers continue to expand the eligibility criteria for living donors. Borderline non-eligibility criteria often include a small mass of the organ and urolithiasis [14–16]. Until recently, the detection of a kidney calculus

in a prospective candidate has been considered a contraindication to donation [17, 18]. However, with the wide use of computed tomography in the examination of living donors, the number of incidentally detected small stones increased to 10% [19, 20].

Over time, the attitude of the transplant community as a whole towards urolithiasis has gradually changed. In 1996, the clinical guidelines of the American Society of Transplant Physicians defined the presence of nephrolithiasis was as a contraindication to lifetime donation due to the subsequent risks for the recipient and donor [18]. Later on, in 2004, at the International Forum on the Care of the Live Kidney Donor in Amsterdam, the asymptomatic presence of a solitary calculus under certain conditions was considered acceptable for discussion in cases of its possible removal during transplantation [12]. A decade later, 84% of the centers agreed with the possibility of lifetime donation in the presence of a history of nephrolithiasis [19, 21].

However, besides nephrolithiasis is associated with certain risks for the donor, a stone in the graft can also create a serious problem for the recipient [18]. Therefore, when taking the decision on extracting such a kidney for the purpose of donation, there are three options for further actions: transplantation of a kidney with a calculus followed by active monitoring; the stone removal from a donor before surgery; and the last method is the stone removal during transplantation [13, 22–24].

The tactics of conservative management of urolithiasis after transplantation is based on the data of some researchers on spontaneous passage of stones less than 4 mm in 60–100% of recipients [7, 11, 19, 25]. There are certain anatomical situations when it is more appropriate to refrain from lithoextraction. For example, if the stone is in a calix with a very narrow neck and the risk of its displacement is negligible [26].

addition, endourological manipulations on the graft are In complicated by impaired topography of the kidney and atypical location of the ureteral orifice. Therefore, it is not uncommon for stones smaller than 15mm to be preferably destroyed by extracorporeal shock wave lithotripsy (ESWL). However, any mechanical impact on the graft, often subject to chronic nephropathy, creates an additional risk of further reduction in its function. In addition, the complete elimination of stones with ESWL is observed only in 40-80% of cases [24]. For extraction or destruction of stones larger than 15 mm, either percutaneous nephrolithotripsy (PNLT) or retrograde intrarenal surgery (RIRS) is more often used. However, retrograde ureterorenoscopy is often difficult due to the high location of the artificial orifice of the graft ureter. Performing percutaneous interventions can also be associated with technical difficulties associated with altered topography of the transplanted kidney and severe perinephric fibrosis. The risk of complications associated both with urolithiasis itself and with interventions to remove stones from the graft is obviously significantly higher than in general urological practice. [24]. Therefore, some centers prefer to remove existing stones ex vivo, that is, when preparing a graft under conditions of cold preservation [10, 26].

So far, clear clinical guidelines have not been developed regarding the management of urolithiasis in living donor transplantation. A.Ganpule et al. suggested using ex vivo ureterorenoscopy or pyelolithotomy for stones with a density of more than 1200 Hounsfield units, or performing RIRS in the donor in advance. At a lower stone density, it is preferable to resort to preliminary ESWL in a low-energy mode [27].

A recent systematic review showed that the pool of living donors with urolithiasis was mainly composed of patients with pelvicalyceal system stones of 1 to 15 mm [28]. Most of the publications describe the "bench surgery" for stone removal, that is, during extracorporeal preparation of the kidney graft for transplantation [11, 12, 19]. The potential advantages of this approach are a low risk of complications for the donor, the reduction of the waiting period for the recipient, and the relatively low cost [29].

According to one of the published reviews, stone removal methods ex vivo distributed as follows: ureteronephroscopy accounted for 82%, pyelolithotomy did for 10% and a combination of these methods for 7 % [28]. In extracorporeal ureterorenoscopy, they resort to extraction with a basket, to pneumatic, ultrasonic or laser destruction. As an endoscopic instrument, a semi-rigid or flexible ureteroscope is used. The choice depends on the size and localization of the calculus [19]. Given the mobility of the ureter, a semi-rigid ureteroscope is usually sufficient; a flexible endoscope is sometimes needed to remove a stone in the lower calyx [26]. Some surgeons prefer the pediatric cystoscope due to its shorter length and, consequently, greater maneuverability [27]. It is possible that HL energy is preferable to pneumatic energy due to a lower risk of mucosal damage in conditions of a non-fixed kidney and stone.

In general, according to a literature review, successful elimination of calculi at "bench surgery" was noted in approximately 96% of cases. The extraction procedure lengthened the duration of the back table surgery for a mean of 30 (1–49) minutes [10]. Difficulties of retrograde intrarenal endoscopic surgery "ex vivo" are caused, among other things, by an impaired spatial orientation and the lack of blood flow in the organ. On the other part, the procedure can be simplified due to free maneuvering of the kidney with a hand [11, 13]. Lack of blood flow and, hence, no tissue bleeding under "bench surgery" conditions contribute to excellent visualization of stones. Some authors consider pyelolithotomy as a good alternative to lithoextraction, mainly in the extrarenal pelvis, or in combination with lithoextraction in a narrow ureter [26, 27].

Meanwhile, the removal of calculi in conditions of "bench surgery" may be associated with certain problems. First, manual-instrumental manipulations with the ureter can lead to damaging its wall. Second, in the absence of blood flow and, accordingly, pressure in the vessels of the kidney, even when using low-flow irrigation, there is a risk of reflux into the venous and the lymphatic system. Reflux in an isolated organ can lead to its edema and ultimately a graft dysfunction. Third, possible damage to the wall of the ureter, pelvis and parenchyma is extremely difficult to determine in the absence of blood flow. In the postoperative period, they can cause complications, for example, urinary fistula or bleeding.

According to a meta-analysis, surgical complications of the early postoperative period occurred in 9 of 92 (9.37%) recipients whose grafts were subjected to extracorporeal stone removal during of the back table surgery. Among them, there are cases of urinary fistulas after ex vivo pyelolithotomy, obstruction of the ureterovesical anastomosis after ureterorenoscopy, hematuria, early dysfunction of the transplanted kidney [11, 28, 30]. In addition, in the long-term period, complications were observed in another 3 (3.1%) recipients from this cohort. However, ex vivo extraction of stones, when identified, remains the predominant method in organ transplantation from cadaveric donors.

There are very few reports in the literature about the preliminary elimination of stones in living donors. Of the 10 cases described, 8 underwent ESWL, one each underwent RIRS and percutaneous nephrolithotripsy (PNLT), respectively [1, 28]. In our series, one donor was subjected to PNLT a month before nephrectomy. We did not experience any difficulties during the nephrectomy and subsequent back table and transplants. It is noteworthy that none of the recipients cited in the literature, who received grafts from living donors previously subjected to lithotripsy or lithoextraction, had complications in the immediate period. Apparently, this could be explained by the kidney removal already after expiry of the period of possible complication development associated with the calculi elimination. First of all, we are talking about the control of residual fragments and the elimination of urinary infection. This approach, however, has two significant drawbacks. First, the staged approach to performing operations leads to an increase in the waiting period for the recipient. Second, and more important, each additional intervention inevitably increases the risk of complications for the donor. Do not forget that the donor is not a patient suffering from any disease, but a volunteer altruist who sacrifices to some extent his health, comfort and time. The number of interventions and their duration can have a critical impact on the decision of a potential donor.

A compromise solution to the problem can be the simultaneous in situ nephrolithotripsy and donor nephrectomy. For the elimination of the calculus in this case, RIRS is best suited. Unlike percutaneous procedures, the retrograde method is not associated with parenchyma damage, which can lead to the development of bleeding, urinary fistula, and even graft rupture in the immediate postoperative period. Meantime, RIRS is performed under "natural" conditions of normal blood flow, and possible tissue damage can be immediately identified and, if necessary, coped with. This approach does not require an increase in the waiting time for the recipient and is not associated with increase in the operation invasiveness and, accordingly, the risk of complications for the donor. After the two simultaneous RIRS and donor nephrectomy described in this article, there were no complications in donors or recipients.

Conclusion

Recruitment of lifetime donors with local urolithiasis allows the increase in the number of related kidney transplants. The presented technique of simultaneous endoscopic retrograde nephrolithotripsy and laparoscopic donor nephrectomy is reproducible, effective and safe. Simultaneous interventions can shorten the donor hospital length of stay and reduce the risk of complications compared to that one in sequential operations.

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