Translational Research in Urology

Home Page: www.transresurology.com

Review

Urolithiasis in Renal Transplantation Patients: An Update of the Literature

Abdolreza Mohammadi[1]*, Mohammad Reza Nikoobakht[2], Seyed Reza Hosseini[2]

[1]*Ebnesina Hospital, Iran University of Medical Sciences, Tehran, Iran*

[2]*Sina Hospital, Tehran University of Medical Sciences, Tehran, Iran*

HIGHLIGHTS

- Diagnostic imaging and therapeutic modalities in transplanted kidneys are similar to normal patients with nephrolithiasis.
- A high index of clinical suspicion is needed for timely diagnosis of urolithiasis in transplant kidneys and early intervention seems crucial.
- The common therapeutic modalities are as same as the normal patients with urolithiasis.

ARTICLE INFO

Receive Date: 17 September 2021

Accept Date: 18 October 2021

Avaliable online: 13 November 2021

DOI: 10.22034/TRU.2021.305308.1081

***Corresponding Author**:

Abdolreza Mohammadi

Email: Ab2rezamohammadi@yahoo.com

Address: Ebnesina Hospital, Iran University of Medical Sciences, Tehran, Iran

ABSTRACT

Urolithiasis is rare in renal transplant patients (<1%). The reasons are multifactorial such as metabolic, medications, and recurrent urinary tract infections. The stones are usually found incidentally on imaging; 50% of these patients are asymptomatic. In some patients' recurrent urinary tract infection (UTI), hematuria, fever, oliguria, or anuria are presenting symptoms. The local pain on the graft may be the only sign. Diagnostic imaging and therapeutic modalities are similar to normal patients with nephrolithiasis. A high index of clinical suspicion is needed for timely diagnosis of urolithiasis in transplant kidneys and early intervention seems crucial. The common therapeutic modalities are the same as the normal patients with urolithiasis.

Keywords: Renal Transplant; Urolithiasis; Percutaneous Nephrolithotomy; Ureteroscopy; Shock Wave Lithotripsy

Introduction

Urolithiasis is uncommon in renal transplant patients (1). The potential reasons are metabolic aberrations, such as metabolic acidosis and subsequent hypocitraturia, urine alkalization due to renal tubular acidosis, and hypercalcemia resulting from secondary hyperparathyroidism (2). Medications such as glucocorticoid may result in hypercalcemia. The other causes of stone formation are foreign bodies (stents and sutures) and recurrent urinary tract infections. The donor kidney may be responsible for urolithiasis (named Donor-gifted stone), although this condition is a rare reason for urolithiasis in a transplanted kidney by routine computed tomography angiography (CTA). In renal transplants, any degree of obstruction can be led to renal failure. Most patients have no specific symptoms, especially renal colic (due to lack of renal innervation in transplant kidney), but some present with UTI, hematuria, and decreased urine output (3-5). It is vital that rising in creatinine level should not be mistaken with transplant rejection. The standard diagnostic imaging modalities can be used in these patients. Therapeutic modalities, including shock wave

lithotripsy (SWL), ureteroscopy (URS), percutaneous nephrolithotomy (PCNL), can be used the same as regular patients with urolithiasis. As a general rule, renal stone <1.5cm can be managed with SWL, but stone >1.5 cm or large stone in the upper ureter cannot be managed by retrograde ureteroscopy due to abnormal location of the implanted ureter, and it can be tackled by percutaneous access.

Methods

By searching performed in databases such as PubMed, Scopus, Embase, Medline, and Web of science with these keywords: renal transplant, urolithiasis, ureteroscopy, percutaneous nephrolithotomy, and shock wave lithotripsy, recent treatment modalities of urolithiasis in renal transplant patients included in our mini-review.

Summary of researches

The stones in the transplanted kidney may be located in the renal system or ureter; stones may be found incidentally or presented with renal failure and hematuria. The consensus is conservative treatment in asymptomatic stone with a size of < 5mm since most of these stones will have expulsed without any harmful event, but most experts agree on active treatment in stone with more than 5 mm.

As mentioned earlier, SWL is the first choice for a renal stone between 5 -15mm, but there are some technical difficulties in performing SWL due to anatomical barrier in iliac fossa that mandates performing SWL in the prone position. For stones >15mm, most studies recommend percutaneous nephrolithotomy as a preferred treatment. Nowadays, with the advance in flexible ureteroscopy design and laser lithotripsy technique, retrograde (retrograde intrarenal surgery) and antegrade approach access to the ureter is a feasible option in stone > 15 mm. The laser lithotripsy is capable of fragmenting any stone. The retrograde approach is the first option, and an integrated approach through percutaneous access is reserved for failed retrograde access. Data about the success of SWL, URS, and PCNL are scarce and mainly upon case series. Data about the success of SWL, URS, and PCNL are scarce and mainly upon case series.

In a multicentric study by Branchereau et al., they reported their experience in the management of urolithiasis in 95 transplant kidney patients; renal stone (51 patients), UPJ stone (16 patients), and ureteral stone (28 patients). Forty-six patients were managed conservatively, so SWL, URS, and PCNL performed in 12, 25, and 10 patients, respectively. Two patients with renal pelvis stone underwent open pyelolithotomy. It is said that the presence of stent may be a risk factor for stone formation, but in this study, the presence of stent (63 patients) was not a risk factor for stone formation compared to stent-less re-implantations (23 patients). Also, the most common type of ureteral reimplant was Lich-Gregoir that may produce difficulty for retrograde access to the ureter; they recommended using the modified Lich-Gregoir technique (lateral displacement of neoureter) for facilitating retrograde access (1).

In a single-center study by Sarier et al., 3758 patients were analyzed retrospectively for eight years. The incidence of urolithiasis was 0.5 % in their report. Among ten patients with renal stones, only one patient underwent PCNL, and the remaining (nine patients) managed with retrograde flexible URS. The most common metabolic abnormalities were hyperparathyroidism and hyperuricemia, respectively. They noted that medication such as cyclosporine is associated with hyperuricemia, but this increase with stone formation is unclear (2).

Cicerello et al., reported an analysis of 953 patients with renal transplants. Ten patients (~1%) had nephrolithiasis; most of them were asymptomatic, seven patients with renal stone, and three with renal stone. Two patients underwent SWL, five patients managed with URS, two patients with PCNL, and open surgery in one patient with impacted lower ureteral stone. The interesting finding in their study was that hyperparathyroidism was the most common metabolic finding (Figure 1). They noted that medication such as cinacalcet hydrochloride, as an inhibitor of parathyroid hormone, can treat this condition, but if medical therapy fails to correct hyperparathyroidism after two years, parathyroid surgery may be needed (3, 4).

There are many debates if the presence of stone in live renal donors prohibits renal transplant. The consensus is that the presence of stone in the renal donor is not a contraindication for renal transplant. There are three options for treating urolithiasis in renal donors; the first is treating urolithiasis in donors before renal transplant, the second is treating stone immediately after nephrectomy and before transplantation, and the last option is treating after transplantation. An exciting study by Rashid et al. reported successful stone treatment in nine renal donors with stone immediately after donor nephrectomy as an ex vivo ureterostomy while renal graft was in chilled normal saline with basketing or in situ laser fragmentation of stone. If we plan to treat renal stones in donors after transplantation, it is recommended that performed with a delay until the dose of the immunosuppressive drug can be reduced (5).

Open surgery is a last resort in treating renal stones in renal transplant patients due to the difficulty of surgery secondary to perirenal fibrosis; the immunosuppressive medication can also increase the risk of urinary fistula formation in open renal surgery in renal transplant.

Krambeck et al., reported their successful experience in 13 patients with renal transplants treated with percutaneous nephrolithotomy. Renal failure, hematuria, and urinary tract infection were the most common presentations. The overall success rate of PCNL was reported similar to the general population. They found that calcium oxalate stone is the most common stone in renal

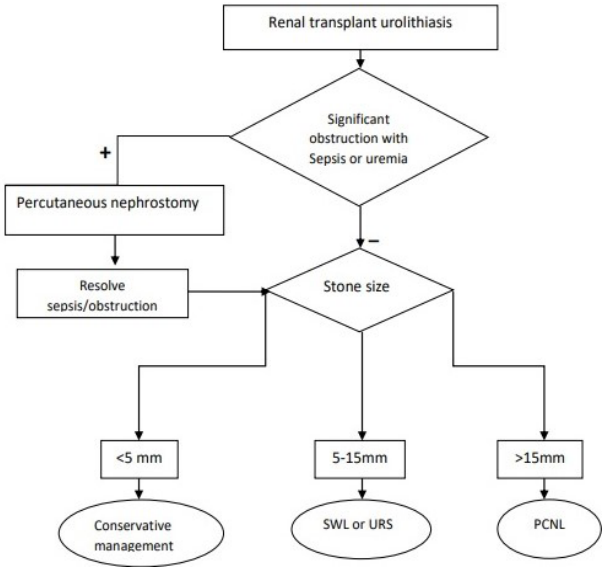

Figure 1. Flowchart of transplanted kidney stones managements. SWL: shock wave lithotripsy, PCNL: percutaneous nephrolithotomy, URS: ureteroscopy

transplant patients. Although hyperuricemia is commonly related to immunosuppressive medication, the incidence of uric acid stone reported only 8% (6).

Retrograde access to the ureter may be difficult in many cases of a renal transplant due to the location of the ureter in the anterior bladder wall, but the use of a flexible ureteroscope overcomes this problem. In a study by Basiri et al., the success rate of retrograde access was reported at 68% in their series. If retrograde access failed, we could use ultrasonography access to the kidney as an alternative approach (7).

There are some technical points in the PCNL of transplant kidneys; due to 180 rotations on its axis, posterior calyces located anteriorly and anterior approach are equivalent to the posterior approach. In a normally located kidney, the patient's position is lithotomy for simultaneous retrograde access. Also, due to fibrous formation around the kidney, experts recommend using telescopic metal dilators. Some experts recommended approaching the lower pole as caudal as possible, whereas others recommended upper pole access to the ability to access the upper ureter simultaneously.

The therapeutic options for ureteral stones in renal transplant are retrograde ureteroscopy, SWL, and antegrade percutaneous access. Nowadays, with the use of flexible ureteroscopy, most patients can be managed with this procedure. Some reports mentioned that lateral displacement of the ureter in ureteroneocystostomy (modified Lich-Gregoir technique) facilitates ureteral access in a retrograde fashion.

Discussion

The therapeutic options for urolithiasis in transplant kidneys are the same for normal kidneys, although the renal function is essential. Obstruction even to a low degree may alter renal function toward failure, so initial management in patients with renal failure is percutaneous drainage with nephrostomy tube, and definite treatment should be postponed till the normal renal function is achieved. If renal function is normal, stone size less than 5 mm, and no significant obstruction, conservative management is recommended. In the study by Serur and colleagues, they followed the patients that had been diagnosed with a renal stone in donated kidney for six years after transplantation, and they had no symptoms, so they recommended that renal transplant is not contraindicated in donors with stone <3mm or with a remote history of stone episodes (> 10 years) (8, 9). If the stone is diagnosed in the rental unit during the renal transplantation process, there are many options, e.g., ex-vivo ureteroscopy on the renal unit after nephrectomy while kidney inserted in normal saline solution ice-slush before transplantation. Wong et al., reported their series on 20 patients with nephrolithiasis during transplantation and treated 17 of them with flexible ureteroscopy and laser fragmentation. Another option is the stone treatment after transplantation when the immunosuppressive dose is reduced (10, 11).

SWL is recommended for stone <15mm in the absence of obstruction, success rate cited between 35 to 70 % in many case reports. In a study by Verrier and colleagues on renal transplant stones in 31 patients, it was shown that about one-third of patients were managed conservatively, in renal stone first minimally invasive treatment was SWL, and if this treatment failed, ureteroscopy or percutaneous treatment was recommended (12-14).

Ureteroscopy is another option for ureteral stone in a retrograde fashion. If retrograde access failed (due to inability to find ureter orifice), the next step would be the antegrade approach. Sevnic et al., reported the success of flexible ureteroscopy with laser lithotripsy in their case series (6 patients). Five patients underwent flexible ureteroscopy (1 renal stone and five ureteral stones), one patient underwent PCNL due to large stone size. All patients were treated successfully with flexible ureteroscopy (15). Percutaneous nephrolithotomy is recommended for stone >15mm or failed endoscopic treatment. Wyatt et al., reported an 81% success rate of PCNL in their series (16 patients). Krambeck et al., reported a 76.9% success rate of PCNL in 13 patients that underwent PCNL (16).

Open surgery is the last option when another minimally invasive fails; due to the effect of immunosuppressive drugs on the healing process, the probability of fistula should be kept in mind.

Conclusion

Due to renal denervation, renal transplant patients do not

experience typical renal colic pain, and many of them are asymptomatic. However, some may be presented with oliguria, uremia, or hematuria, so a high index of suspicion is needed to diagnose urolithiasis in renal transplant patients. Immediate intervention is essential for preserving renal function in obstructed renal unit. Diagnostic modalities are similar to normal patients. If there is an infection or significant obstruction first step of treatment is percutaneous nephrostomy, and definite treatment should be postponed to stabilize patients. Therapeutic modalities are similar to normal patients. For renal stone<5 mm, the consensus is expectant management, stones 5-15mm may be treated with SWL, and for stones >15mm, PCNL is recommended. Open surgery was the last option when the other options failed, simultaneous ureteral stone and ureteral stricture that need surgical correction and staghorn stones.

Authors' contributions
All authors contributed equally.

Acknowledgments
Special thanks to the Urology Research Center (URC), Tehran University of Medical Sciences (TUMS).

Conflict of interest
All authors declare that there is not any kind of conflict of interest.

Funding
There is no funding.

Ethical statement
Not applicable.

Data availability
Data will be provided by the corresponding author on request.

Abbreviation

CT	Computed tomography
CTA	Computed tomography angiography
PCNL	Percutaneous nephrolithotomy
SWL	Shock wave lithotripsy
URS	Ureteroscopy
UTI	Urinary tract infection

References

1. Branchereau J, Timsit M, Neuzillet Y, Bessède T, Thuret R, Gigante M, et al. Management of renal transplant urolithiasis: a multicentre study by the French Urology Association Transplantation Committee. World journal of urology. 2018;36(1):105-9.
2. Sarier M, Duman I, Yuksel Y, Tekin S, Ozer M, Yucetin L, et al. Ex vivo stone surgery in donor kidneys at renal transplantation. International Journal of Urology. 2018;25(10):844-7.
3. Cicerello E, Merlo F, Mangano M, Cova G, Maccatrozzo L. Urolithiasis in renal transplantation: diagnosis and management. Archivio Italiano di Urologia e Andrologia. 2014;86(4):257-60.
4. Aghamir SMK, Salavati A, Hamidi M, FallahNejad A. Primary Report of Totally Tubeless Percutaneous Nephrolithotomy Despite Pelvi-calyceal Perforations. Urology journal. 2017;14(4):4020-3.
5. Rashid MG, Konnak JW, Wolf JS, Punch JD, Magee JC, Arenas JD, et al. Ex vivo ureteroscopic treatment of calculi in donor kidneys at renal transplantation. The Journal of urology. 2004;171(1):58-60.
6. Krambeck AE, LeRoy AJ, Patterson DE, Gettman MT. Percutaneous nephrolithotomy success in the transplant kidney. The Journal of urology. 2008;180(6):2545-9.
7. Basiri A, Simforoosh N, Nikoobakht MR, Moghadam MMH. The role of ureteroscopy in the treatment of renal transplantation complications. Urology journal. 2009;1(1):27-31.
8. Serur D, Charlton M, Juluru K, Salama G, Locastro E, Bretzlaff G, et al. Long term follow up of kidney donors with asymptomatic renal stones. Nephrology. 2017;22(8):649-51.
9. Narouie B, Saatchi M. Short term and Long-term Survival Rate and Risk Factors of Raft Rejection after Deceased Donor Kidney Transplantation: A Systematic Review and Meta-Analysis. Translational Research Urology. 2021:-.
10. Wong KA, Olsburgh J. Management of stones in renal transplant. Current opinion in urology. 2013;23(2):175-9.
11. Aghamir SMK, Heshmat R, Ebrahimi M, Ketabchi SE, Dizaji SP, Khatami F. The impact of succinate dehydrogenase gene (SDH) mutations in renal cell carcinoma (RCC): A systematic review. OncoTargets and therapy. 2019;12:7929.
12. Verrier C, Bessede T, Hajj P, Aoubid L, Eschwege P, Benoit G. Decrease in and management of urolithiasis after kidney transplantation. The Journal of urology. 2012;187(5):1651-5.
13. Aghamir SMK, Jamali R, Tamehri Zadeh SS, Khajavi A, Khatami F, Pourmand G, et al. The Relationship between Graft Function and Liver Function after Kidney Transplantation: A Retrospective Cohort Study. Translational Research Urology. 2019;1(2):84-90.
14. Aghamir SMK, Elmimehr R, Modaresi SS, Salavati A. Comparing bleeding complications of double and single access totally tubeless PCNL: is it safe to obtain more accesses? Urologia internationalis. 2016;96(1):73-6.
15. Sevinc C, Balaban M, Ozkaptan O, Karadeniz T, editors. Flexible ureterorenoscopy and laser lithotripsy for the treatment of allograft kidney lithiasis. Transplantation proceedings; 2015: Elsevier.
16. Wyatt J, Kolettis PN, Burns JR. Treatment outcomes for percutaneous nephrolithotomy in renal allografts. Journal of endourology. 2009;23(11):1821-4.

Author (s) biosketches
Mohammadi A, MD, Ebnesina Hospital, Iran University of Medical Sciences, Tehran, Iran.
Email: Ab2rezamohammadi@yahoo.com
Nikoobakht MR, MD, Sina Hospital, Tehran University of Medical Sciences, Tehran, Iran.
Email: Nikoobakht_r@live.com
Hosseini SR, MD, Sina Hospital, Tehran University of Medical Sciences, Tehran, Iran.
Email: srhoseini@tums.ac.ir

How to cite this article
Mohammadi A, Nikoobakht MR, Hosseini SR. Urolithiasis in Renal Transplantation Patients: An Update of the Literature. Translational Research in Urology. 2021 Nov;3(4):149-153.
DOI: 10.22034/TRU.2021.305308.1081
URL: https://www.transresurology.com/article_138973.html