DOI: 10.15825/1995-1191-2023-3-57-63

EFFICACY OF EXTRACORPOREAL SHOCK WAVE LITHOTRIPSY FOR POST-TRANSPLANT KIDNEY STONES. HOPE OR DISAPPOINTMENT?

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Nephrolithiasis in a transplanted kidney is an important medical and social problem. The presence of renal calculi may not manifest clinically for a long time due to the peculiarities of the surgical intervention during organ transplantation. Development of chronic urinary tract infection and deterioration of the functional ability of the renal transplant in the presence of kidney stones can lead to graft death, which is an immediate threat to the patient's life. Existing Russian guidelines on the treatment of urolithiasis currently lack a clear strategy for the management of kidney transplant recipients. **Objective:** to systematize literature data on analysis of the outcomes of extracorporeal shock wave lithotripsy (ESWL) and other methods in patients with post-transplant kidney stones. **Results.** Thirty-five publications on the research topic were selected. We summarized the information on various therapy options for patients with stones in transplanted kidney: endourological approach, ESWL, percutaneous nephrolithotripsy (PCNL), open surgical treatment (nephrostomy, pyelolithotomy). A modern foreign algorithm for the management of patients with post-transplant kidney stones depending on the severity of obstruction with sepsis and the size of the renal calculi is presented. **Conclusion.** 1. The presence of stones in a kidney graft is a clinical situation that requires surgical treatment. 2. In clinical practice, different methods of treatment can be used, such as open intervention, ESWL, PCNL, retrograde transurethral manipulations. 3. In most cases, patient management tactics depend on the clinical picture (presence/absence of obstruction) and the size of the calculi. 4. The use of ESWL, as the most frequently used method, testifies to its efficiency and low-traumatic effect.

Keywords: graft, nephrolithiasis, extracorporeal shock wave lithotripsy, ureteroscopy, percutaneous nephrolithotripsy.

INTRODUCTION

Stone formation after kidney transplantation is a possible transplant complication, and can lead to chronic pyelonephritis, hydronephrosis, anuria, graft dysfunction and graft loss [1, 2]. Foreign researchers have noted that in 0.2–5.7% of cases after kidney transplantation, stones are verified in the kidney. An analysis of a retrospective study by Russian authors (1,024 cases of renal transplants) indicates the detection of renal calculi in 1.4% of the cases [3, 4]. Based on data from a large study (1994–1998) on the prevalence of nephrolithiasis in renal transplant recipients with the participation of 42,000 patients, Kevin et al. revealed that women tend to develop this complication more frequently [5].

Data from a meta-analysis by Cheungpasitporn et al. suggest that calcium salts (oxalate and phosphate) are the basis of stones in the vast majority of cases [6, 7]. The incidence of urate ranges from 0.2–10% [8].

Some researchers have suggested that renal calculi are more likely to occur within the first year after transplantation, but there has been a case reported where it took 17 years. Nephrolithiasis detected at the time of transplantation reflects cases of donor-associated nephrolithiasis and accounts for about 7% of all cases of kidney transplant nephrolithiasis [9].

Kidney graft recipients with nephrolithiasis require increased attention because of changes in kidney function and kidney innervation. A wait-and-see conservative approach to the management of patients with renal calculi <4–6 mm involves strict clinical, radiological and laboratory monitoring [7–9]. Possible therapy options include endourological approach, ESWL, PCNL and open surgical treatment (nephrostomy, pyelolithotomy)

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[10]. Existing Russian guidelines on the treatment of urolithiasis contain no clear strategy for the management of patients with transplanted kidney [12]. Therefore, the actual task is to analyze the Russian and foreign experience of various approaches to the treatment of such patients. This served as the basis for our literature review.

The **purpose** of this work is to systematize the literature on the issue of ESWL and other methods of treatment for kidney transplant stones.

MATERIALS AND METHODS

Medical literature was searched using the information and analytical databases Cochrane, Medline (part of the PubMed search engine), elibrary using text search queries "kidney transplantation", "stones in transplanted kidney", "extracorporeal shock wave lithotripsy of transplanted kidney", and "ESWL of transplanted kidney". Literature sources found were taken for further analysis according to the following criteria: date of publication, from 2000 to 2022; type of publication (in descending order of importance), meta-analyses, systematic reviews, results of randomized and non-randomized trials, registry data. A total of 35 publications meeting the inclusion criteria were selected based on the search results and were used in the analysis.

RESULTS

When analyzing the sources that were selected for writing the review, we initially considered the works that confirmed the fact that open surgical intervention in this clinical situation is considered by the researchers as an extreme measure due to the complexity and traumatic nature of the intervention [10–13]. Other approaches to the management of such patients (endourological, PCNL were less frequently considered by the authors when choosing the kidney graft stone treatment method [14–16]. The ESWL method, as the most frequently used in clinical practice, allows noninvasive intervention that does not require general anesthesia [17–19]. The use of ESWL in clinical practice demonstrates the prevalence and demand for its use, including in a special category of patients with renal transplant calculi [17–19]. Thus, in a 2006–2009 study performed at Vladimirsky Moscow Regional Research and Clinical Institute, ESWL (32 sessions) was performed in 14 patients with urolithiasis (stone size varied from 8 to 15 mm) of the transplanted kidney (the period after transplantation was from 6 months to 2 years). Evaluation of the functional state of the graft, according to the data of laboratory research methods, confirmed the feasibility of ultrasound-guided ESWL on renal calculi in this category of patients in order to prevent complications [20].

Studies by Russian scientists have confirmed the fact that ESWL is a low-traumatic procedure and comes with no side effects. Seventeen lithotripsy sessions were performed in 8 patients. Each patient had two sessions; one patient had three. Stones were detached within 1–2 weeks. No adverse reactions were detected. The efficacy of the method used was registered in all patients in 100% of cases [3].

The efficacy of ESWL, depending on stone size, location and number, was studied in the work of Spanish researchers led by Millán Rodríguez. They analyzed a cohort of patients with renal transplantation, in which 60% of the patients had multiple stones; stones were localized in the ureter (ureterovesical anastomosis) in 53% of patients, and in the bladder in 13% of patients. The authors found that the best results were achieved with a single stone, up to 13 mm in size, localized in the lower ureter [21].

In an analysis of data from 19 patients, Klingler et al. also reported the effectiveness of ESWL for caliceal stones sized 5 to 15 mm. If the stone diameter exceeded 15 mm, it was recommended to PCNL or retrograde ureterolithotripsy [22]. The same approach to the management of recipients with renal calculi in a transplanted kidney was demonstrated by Sha-dan et al. in their retrospective analysis of data from 1979–2009 [4]. A review by Challacombe et al. described 13 patients who underwent ESWL, with eight patients requiring several sessions and two patients requiring additional ureteroscopy (URS) [23].

In a study by Yuan et al., additional ESWL sessions were performed in 4 out of 5 patients, and the authors noted that due to the ectopic location of the renal graft, the pelvic bones may interfere with stone visualization and reduce the effectiveness of this treatment procedure [24].

Several published reports have recommended PCNL and antegrade endourological manipulations as the most effective methods of nephrolithiasis treatment in renal transplant recipients regardless of the stone size and its localization. For example, foreign researchers in their work summarized the results of PCNL (4760). The clinical situations considered by the authors included patients with staghorn calculi (1240), ureteric stones (85), and transplanted kidneys (14). A study of these patients with stones in transplanted kidneys demonstrated a positive effect in 89% of cases [25]. In 2013, researchers Ji et al. reported the high effectiveness of minimally invasive percutaneous laser nephrolithotripsy in 11 patients with renal transplantation [26].

There have been works that presented good outcomes of treatment of graft calculi via retrograde URS, for instance, the study by Basiri et al. [27]. Hyams et al. reported their experience with 12 patients treated exclusively by ureteroscopic intervention, seven by retrograde access and five by antegrade access, with complete stone removal achieved in 11 of 12 patients by this surgical intervention [28]. Branchereau et al. performed a retrospective review of 95 patients with graft calculi treated at 11 renal transplant centers located in different European countries. Urethroscopy was performed in 26%

of patients with a 6–24 mm stone, and no graft loss or mortality was reported with an average follow-up of 72 months [11].

In 2019, Sarier et al. reported the use of minimally invasive surgical treatment of allograft lithiasis in 22 patients, including flexible and semi-rigid URS and PCNL, without developing serious postoperative complications and with complete stone removal in 89% of cases [29].

In the work by Rebecca et al. summarized data on 2652 patients (follow-up period 2009–2020), 18 of whom underwent URS for transplanted kidney or ureteral stones; most procedures were performed using retrograde approach. In 16 of the 18 patients, a single procedure was sufficient for complete elimination of the calculus [30].

In 2012, Romain Boissier et al. performed a retrospective analysis of 37 studies involving 553 patients who underwent 20 antegrade URS, 154 retrograde URS, 118 PCNL, 25 open surgical interventions, and 155 ESWL; conservative management of patients was performed in 140 cases. The researchers noted that the stone-free rate after the procedure was 96% with open surgery, 95% with antegrade URS, 86% with PCNL, 81% with retrograde URS, and 75% with ESWL [31].

In a 2018 publication describing more than 30 years of experience in the treatment of stones after kidney transplantation based on data from 29 studies that included 42,096 patients, treatment modalities were ESWL (43.1%), active surveillance (25.4%), retrograde URS (17.6%), antegrade URS (3.9%), percutaneous nephrolithotomy (3.9%), open approach (3.9%), and urine alkalinisation (2%) [32].

A paper by X. Li et al. summarized the results of 29 studies devoted to the management of patients with stones in the renal graft; the choice of treatment tactics was determined by the clinic, localization and size of stones. The authors concluded that the use of minimally invasive procedures is optimal, and two or more such procedures can be used to increase the effectiveness of treatment and accelerate recovery processes in the postoperative period [10].

DISCUSSION

There are a number of causes of formation of stones in a graft, such as thyroid dysfunction (imbalance of hormones T3, T4), ureteral obstruction accompanied by urinary stasis, presence of a foreign body (for example, non-absorbable suture material), metabolic disorders (gout, hyperuricemia, etc.) [12]. Continuous intake of medications such as immunosuppressants increases serum and urine uric acid levels, which may also lead to stone formation. Some researchers have reported an association between stone formation after kidney transplan-

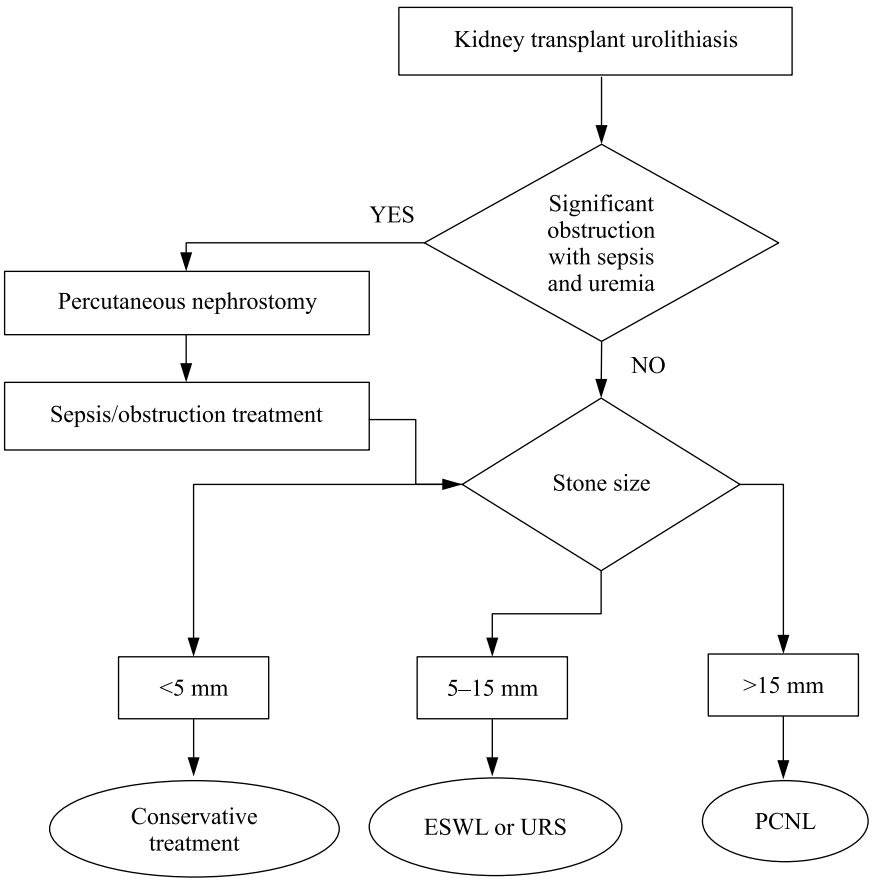

Fig. Flowchart of management of kidney transplant recipients with kidney stones (Adapted from Mohammadi, 2021 [36])

tation and age, gender, and tobacco smoking in donors and recipients [33, 34].

Changes in the treatment tactics for patients with renal calculi is worth noting. Initially, when the pathological process was asymptomatic, preference was given to conservative management, including dynamic monitoring and ultrasound examination of the kidneys. Later, removal of stones from the transplanted kidney even in the absence of clinical symptoms in the recipient was considered optimal. Proponents of this approach explain its prospects by the steady deterioration of the function of the transplanted kidney and the development of chronic urinary tract infection in the presence of renal calculi, which could eventually lead to graft death [35].

Determining the approach to surgical treatment tactics is a complex task, since many factors need to be taken into account: the polyetiology of the pathology, concomitant changes in the graft tissue, ongoing therapy, etc.

Initially, open techniques (nephrostomy, pyelolithotomy) were popular. However, it should be emphasized that open surgical intervention has a number of drawbacks: preparation of the kidney and ureter is a difficult task due to their topographical features; postoperative complications (infection, fistula formation, pain syndrome, etc.) are possible [11, 13]. In addition, open surgical intervention can be associated with pronounced cicatricial adhesion around the transplanted kidney.

The use of ESWL (as both monotherapy and combined treatment) in clinical practice is justified and effective for kidney and ureteral stones ≤1.5 cm in size. For calculi >1.5 cm, this technique is usually combined with renal catheterization, placement of an internal stent or (less frequently) percutaneous puncture nephrostomy (Fig.) [12].

CONCLUSIONS

1. The presence of kidney stones in kidney transplant recipients is a clinical situation that requires surgical treatment.
2. In clinical practice, different treatment methods can be used: open intervention, ESWL, PCNL, retrograde transurethral manipulations.
3. In most cases, patient management tactics are determined by the clinical picture (presence/absence of obstruction) and size of the calculi.
4. The use of ESWL, as the most common method, testifies to its effectiveness and low traumaticity.

The authors declare no conflict of interest.

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The article was submitted to the journal on 5.04.2023