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Original article

A consecutive series of patients undergoing trans-urethral cystolithotripsy with ballistic lithotripsy by a tertiary referral center for neurogenic bladder

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Summary. *Background and aim of the work:* Patients with neurogenic bladder (NB) have an increased risk of developing bladder stones due to bladder catheter, incomplete bladder emptying, recurrent urinary tract infections, and immobilization. In these patients, minimally invasive treatments are usually adopted, as non-invasive extracorporeal shockwave lithotripsy is limited by the risk of not clearing all stone fragments, and open surgery is usually discouraged. The aim of our study was to present our experience with trans-urethral cystolithotripsy (TUCL) in patients treated by a tertiary referral center for NB. *Methods:* We retrospectively collected pre-, intra- and post-operative data from our patients, who underwent TUCL from October 2013 to October 2019. The procedure was performed with a 24 Fr cystoscope and a ballistic lithotripter. Lapaxy was performed with Ellik bladder evacuator. All procedures were performed by two expert surgeons. Stone-free rate (SFR) was defined as the percentage of patients with absence of residual fragments >2 mm in diameter. *Results:* We performed consecutively 91 TUCLs in 75 patients during the selected period. SFR was 94.1%. Intra- and post-operative complications occurred in one (1.1%) patient. Our statistical analysis outlined the SFR was affected in a statistically significant way by sex, NB etiology, stone cumulative diameter, and operative time. *Conclusion:* Our series proved the safety and efficacy of TUCL with ballistic lithotripsy in NB patients. Further multicenter randomized controlled trials are mandatory to validate definitively TUCL as the gold standard therapy for bladder urolithiasis in NB patients, and to identify risk factors limiting the SFR. (www.actabiomedica.it)

Key words: ballistic lithotripsy, bladder stone, neurogenic bladder, trans-urethral cystolithotripsy, spinal cord injury, trans-urethral cystolithotripsy

Background and aim of the work

After spinal cord injury (SCI), the loss of sensory and motor function causes the onset of a neurogenic bladder (NB) and secondary urologic complications including renal failure, bladder cancer, urinary tract infection (UTI), incontinence, and morphologic alterations of bladder and urethra (1).

Patients with neurogenic bladder (NB) have, also, an increased risk of developing bladder stones due to bladder catheter, incomplete bladder emptying, recurrent UTIs, immobilization and hypercalcuria (2). Bladder stones can cause recurrent urinary tract infections, hematuria, catheter malfunction, vesical chronic inflammation, and autonomic dysreflexia in SCI patients with a level of injury above T6 (3-4).

NB patients pose frequently a particular challenge because of their multiple comorbidities, skeletal deformities, previous surgeries, urinary diversions and chronic asymptomatic bacteriuria. In these patients, minimally invasive treatments are usually adopted (5), as noninvasive extracorporeal shockwave lithotripsy (ESWL) is limited by the risk of not clearing all stone fragments (6), and open surgery is usually discouraged because of fragility in severe baseline conditions, like spinal cord injury (SCI), myelomeningocele (MMC) etc.

The aim of our study was to present our experience with ballistic trans-urethral cystolithotripsy (TUCL) and to prove the safety and efficacy of this technique in BN patients treated by a tertiary referral center.

Methods

We retrospectively collected data from our NB patients (who performe clean intermittent catheterization), who underwent TUCL from October 2013 to October 2019 by our center, after the diagnosis of bladder lithiasis with abdomen ultrasound, to which patients were subjected annually. All data were collected in compliance with privacy laws. Each patient remained anonymous and was associated with an identification number; we did not disclose any sensitive data.

All procedures were performed by two expert surgeons at the end of their learning curve. We administered peri-operative antibiotic prophylaxis with a third-generation cephalosporin, or with aminoglycoside in case of allergy. Stone burden was estimated endoscopically at the beginning of the procedure by I operator in order to limit inter-operator variability with ultrasound (US) scan, the most common preoperative exam.

The procedure was performed with a 24 Fr cystoscope and a ballistic lithotripter, called Wolf 2290 LITHOCLAST (Richard Wolf GmbH, Germany). The 1.6-mm-large probe was adopted. The pressure ranged 1.0-1.5 bar, while the frequency was 12 Hz. Lapaxy was performed with Ellik bladder evacuator. At the end of the procedure, we placed a silicone two-way bladder catheter.

We collected pre-, intra- and post-operative data. Stone-free rate (SFR) was defined as the percentage of procedures ending with absence of fragments > 2 mm in diameter and/or no need of additional procedures after one month from surgery.

As for statistical analysis, we estimated median and interquartile range (IQR) for each quantitative variable, while we reported the occurrence of the various outcomes for qualitative variables. Data were stored and analyzed using Microsoft Excel (Microsoft Corporation, Washington, USA). Later, we statistically evaluated the correlation between SFR and all other variables collected with Statistical Package for Social Science (SPSS), version 20.0 (IBM, New York, USA). Statistical significance was set as p value < 0.05.

Results

In Table 1 we reported all data of our 91 TUCLs performed consecutively in 75 patients (65 males and 10 females) from October 2013 to October 2019. In 7 patients, bladder stones relapsed and they underwent a novel TUCL; among them, a 3rd TUCL was performed in 3 patients. The median stone number and stone cumulative diameter were, respectively, 1 (range: 1-5) and 20 mm (range 6-86 mm). The median operative time (OT) was 40 min (range: 20-150 min).

Intraoperative and postoperative complications were reported only in the same one patient (1.1%), who was affected by macrohematuria. The length of hospitalization was 1 day after 89/90 TUCLs and 7 days in the patient who presented macrohematuria intra- and post-operatively, treated only with cystolusis with a complete resolution of the emathuria.

The SFR after the 1st TUCL was 94.5% (80/85); the SFR after a second- and third-look (performed approxinately after 30 days from the last procedure) were, respectively, 98.8 % (84/85) and 100% (85/85). Four patients underwent a II look: 2 men vs. 2 women; 2 patients with MMC vs. 2 patients with SCI. One female patient with MMC underwent a III look. The median follow-up was 29 mounths (range 60-3 mounth).

In Table 2, we screened statistical relationships between SFR and all collected parameters. SFR was significantly affected by sex (p=0.048), NB etiology

Table 1. Pre-, intra- and post-operative data collected from our consecutive series of patients with neurogenic bladder undergoing trans-urethral cystolithotripsy.
Acronyms: IQR = interquartile range; MMC = myelomeningocele; SCI = spinal cord injury; SFR = stone-free rate; TUCL = trans-urethral cystolithotripsy

Data	Value
No. TUCL	91
No. patients	75
Age median (IQR)	43.5 (30-57.5)
Sex	Males: 65 (86.7%) Females: 10 (13.3%)
Neurogenic bladder: Etiology	SCI above C8: 36 (48%) SCI below T1: 30 (40%) MMC: 5 (6.7%) Iatrogenic: 3 (4%) Multiple Sclerosis: 1 (1.3%)
Stone number median (IQR)	1 (1-3)
Stone cumulative diameter median (IQR)	20 mm (14.75-28.5 mm)
Operative time median (IQR)	40 min (30-60 min)
Intra-operative complications	Macrohematuria: 1 (1.1%)*
Post-operative complications	Macrohematuria: 1 (1.1%)*
Length of stay median (range)	1 day (1-7 days)*
SFR after 1st TUCL	94.1% (80/85)
SFR after 2st TUCL	98.8% (84/85)
SFR after 3st TUCL	100% (85/85)

* The length of stay was 1 day after 89/90 TUCLs and 7 days in the patient who presented macrohematuria both intra- and post-operatively.

(p=0.018), stone cumulative diameter (p=0.002), and operative time (p=0.010).

Discussion

Bladder stones are a common urological complication in patients with NB. The incidence of bladder stones varies depending on the bladder management. Indwelling bladder catheters (iBC) are associated with a high risk of stone formation with an incidence of 46-53% (7-8). Ord et al. demonstrated that the absolute annual risk of stone formation in patients with an iBC is 4% compared to 0.2% for those on clean intermittent catheterization (CIC). In patients treated for previous stones, the risk of forming a subsequent stone quadruples to 16% per year. Bladder stones are no more likely to form in patients with suprapubic catheters compared to those with indwelling urethral catheters (7-9). The increased risk of bladder stones formation occurs independently of age, sex and injury level (7). Vesical lithiasis is related to incomplete bladder emptying, recurrent UTIs, immobilization and hypercalcuria (2).

The current surgical strategy for bladder stones in patients with NB is represented by TUCL with different lithotripsy methods, e.g. electrohydraulic lithotripsy (EHL), Holmium:YAG laser, US or ballistic probes. Open cystolithotomy is now restricted to voluminous bladder stones. In our center, we use a cystoscope with ballistic lithotripsy and try to limit high bladder pressures, which may provoke UTI, vesicoureteral reflux, mucosa injury, bladder perforation, autonomic dysreflexia in SCI patients with a level of injury above D6,

Table 2. Analysis of statistical differences in terms of stone-free status considering single parameters. Statistically significance (*) was set as p value < 0.05

Parameters	Stone-free status		p value
	Yes	No	
Age mean rank	43.5	32	0.381
Sex - Males - Females	 70 11	 2 2	0.048*
Neurogenic bladder: Etiology - SCI above C8 - SCI below T1 - MMC - Iatrogenic - Multiple Sclerosis	 40 33 4 3 1	 1 1 2 0 0	0.018*
Stone number mean rank	2.9	1.5	0.273
Stone cumulative diameter mean rank	27.1	52.8	0.002*
Operative time mean rank	41.6	72.4	0.010*
Intra-operative complications	-	-	1.000
Post-operative complications	-	-	1.000
Length of stay mean rank	1	1	1.000

featured by severe hypertension, pulmonary edema, hemorrhagic stroke, myocardial infarction and, even, posterior reversible encephalopathy syndrome with high risk of mortality (10).

Following our approach, we reported a high SFR (94.1%), which raised up to 98.8 and 100%, respectively, after a second- or a third-look TUCL. Our SFR was similar to the data reported in literature (11).

According to our experience, the SFR was significantly affected by sex, NB etiology, stone cumulative diameter and OT. Worse outcomes in women may a bias due to small representation of this population compared to men (10 vs. 65 cases). Evaluating different percentages of SFR per each NB cause, MMC is associated with the worst SFR. This condition affects people from intra-uterine life, influencing organ growth from the very beginning. In these patients, it is common to find severe morphologic alterations of bladder and urethra which favor stone formation and limit surgical treatments. Stone cumulative diameter and OT influence SFR, as high stone burden is associated with increased OT itself, and necessity to stop the procedure, continuing it in a II session.

We recorded a very low rate of complications (1.1%), with only one case of persistent macrohematuria with consequent suspension of the surgery and prolonged hospital stay from 1 (standard) to 7 days. Neither cases of autonomic dysreflexia nor post-procedural sepsis occurred, maybe due to the peri-operative wide-spectrum antibiotic prophylaxis and the low bladder pressures maintained intra-operatively. The complication reported is classified as I grade of Clavien-Dindo scale. Our rate is lower than others reported in literature. Eyre et al. registered an overall complication rate of 17% following TUCL in SCI patients (12). Among the most frequent complications reported in literature, the lithotripsy devices may cause some degree of collateral bladder mucosal damage, increasing the risk of macrohematuria or perforation (13).

Alternative forms of lithotripsy have been used in similar frail patients over the years. Even if it is a non-invasive method, ESWL poses difficulties with

the drainage of stone fragments generated by shock waves (6-14). The advent of the Holmium:YAG laser for treating ureteric and renal stones has provided a method of fragmentation also for bladder lithiasis (15), but it is much more expensive. Some studies compared the use of Holmium:YAG laser with LithoClast as lithotripsy device: they reported that both lithotripters were safe and effective to fragment the bladder stones with a similar SFR after the first session (16). Open cystolithotomy, reserved for voluminous stones, in SCI patients is linked to an high rate of post-operative complications; therefore, clinicians may prefer more sessions of TUCL rather than one-session open surgery in a frail population like ours.

The best strategy to diagnose bladder stones precociously, treat them endoscopically and limit the rate of complications is represented by an annual abdomen US screening in patients with NB, which should be mandatory in the follow-up visits (17).

Our study reports some limits. As a single-center retrospective study with a small population, in which patients had a variable duration of follow-up, this paper is associated with a low level of evidence. Therefore, variables affecting SFR should be confirmed through further multi-center studies enrolling large samples. The superiority of ballistic lithotripsy over other techniques, like Holmium:YAG laser, should be investigated through randomized controlled trials. Stone burden and stone-free status were assessed endoscopically intra-operatively by the surgeon, and not through a computed tomography scan which is objective and not related to inter-operator variability.

Moreover, some data lack. For example, we do not routinely analyze the composition of the removed stones on the assumption that the majority of them were infection-related in etiology (18), given that the NB patients were managed with CIC and the were exposed to chronic bacterial colonization of the bladder.

Our study reported excellent outcomes with a low-cost equipment, made up of a rigid cystoscope and a low-powerful ballistic lithotripter. Considering the increased incidence of bladder stones and raising prevalence of patients with NB in underdeveloped countries, our methodology may serve as a reference for urological services with restricted resources.

Conclusion

In conclusion, our series proved the safety and efficacy of TUCL with ballistic lithotripsy in NB patients. The SFR proved to be negatively affected by female sex, MMC, stone cumulative diameter, and OT. Further comparative randomized controlled trials are mandatory to validate definitively TUCL as the gold standard therapy for bladder urolithiasis in NB patients, and to identify risk factors limiting the SFR.

Conflict of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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