Methodological Review by Timothy Y. Tseng, MD

Article Reviewed

Basiri A et al. A Multicenter, Randomized, Controlled Trial of Transureteral and Shock Wave Lithotripsy—Which is the Best Minimally Invasive Modality to Treat Distal Ureteral Calculi in Children? J Urol 2010; 184:1106-10

Review

Although both ureteroscopy (URS) and shock wave lithotripsy (SWL) are accepted treatment modalities for urinary calculi in children, due to the particular anatomic constraints associated with operating on children, SWL has historically been favored. Further miniaturization, however, has made URS more feasible in children. Basiri et al. performed a randomized controlled trial comparing URS to SWL in 100 children. Stone-free rates were assessed at discharge, 2 weeks, and 3 months. The need for repeat procedures and complications were also assessed.

Are the results valid?

This multi-center randomized controlled trial addresses the clinical question of whether ureteroscopic lithotripsy or SWL is more effective for the treatment of distal ureteral calculi in children. Although randomization was reported, it is unclear what the “randomized numerical schedule” was and how it was distributed. The apparent exclusion of some female children from SWL after randomization also raises questions about the method of randomization. Whether patients were also analyzed in an intention-to-treat fashion was not addressed by the authors. Although it is difficult to blind surgeons and possibly patients to the procedure performed, blinding of the outcomes assessors was not reported.

Determinations of stone-free status were accomplished by ultrasound at 2 weeks and by excretory urography at 3 months with unspecified variations to accommodate patients with residual stone burden. The difference in sensitivity of these studies could potentially have led to decreased detection of residual stone burden, particularly for the treatment group that may have had a lower residual burden in the first place (URS). Of note, the method of determination of stone-free status at the time of discharge was not specified. On a positive note, the authors reported 100% follow-up, an attempt was made to standardize follow-up and detection of residual stone burden and the trial was not stopped early.

In summary, the lack of complete documentation of the methodology of the trial casts some doubt on the validity of its results. If the GRADE framework\(^1\) for rating the quality of evidence were used, the quality of evidence in this study would be downgraded to “low,” indicating increased uncertainty that these results reflect “the truth”.

What are the results?

Based on Table 1, the two groups appeared largely comparable in terms of patient age, stone size, and known prognostic variables. Mean age of patients was 6.5±3.9 years for URS and 5.5±4.7 years for SWL. The authors found statistically significant differences in stone-free rates between ureteroscopic lithotripsy and SWL, with URS affording an approximately 20% advantage over SWL at all time points. At 3 months, among patients who had undergone only 1 procedure, stone-free rates were 82% (41/50) for
URS and 62% (31/50) for SWL (p=0.001). This equates to a relative risk of 1.32 (95% CI 1.03 – 1.70) of being stone-free after URS when compared to SWL, an absolute risk increase of 0.2 (0.02 – 0.36), and a number need to treat of 6 (3 – 42).² These numbers suggest a definite advantage of URS versus SWL. However, there appears to be considerable uncertainty about the magnitude of this benefit. This lack of precision is a reflection of the relatively small sample size and absolute number of events.¹

Equal consideration should be given to assessment of harms. Two ureteral perforations occurred in the URS group, one of which was treated with an open repair. SWL resulted in significantly more minor complications such as skin bruising. Interestingly, the mean length of post-op hospitalization was significantly greater for URS at 36 hrs compared to 12 hrs for SWL (p=0.003). Satisfaction rate, which appeared to be defined as a preference for having the same procedure repeated in the future, was significantly higher for URS at 94% compared to SWL at 80% (p=0.004).

In summary, when comparing URS versus SWL for distal ureteral stones, URS appears to be associated with a clinically important advantage of uncertain magnitude, an increased risk of serious harm (ureteral perforation), and a longer length of stay.

Can the results be applied to patient care?

Although the most recent AUA guidelines suggested that anatomical limitations in children favor SWL,³ this study suggests that an ureteroscopic approach is both feasible and significantly more efficacious than SWL in children. Ureteral perforation did occur at a rate of 4% in the URS arm. However, this is consistent with data from the adult literature indicating a perforation rate of < 5%. One caveat is that this study utilized pneumatic lithotripsy for the majority of the URS patients. In many institutions, laser lithotripsy is favored. Indeed, as the guest editorial comment indicated, laser lithotripsy has been retrospectively evaluated and found to have a similarly low complication rate.⁴ Nevertheless, this study demonstrates that ureteroscopic access can be obtained reliably in pediatric patients. Because ureteral stricture may be considered catastrophic in pediatric patients, open discussion of the risks involved with a patient’s parents should precede any decision on choice of intervention.

References

Clinical Review by John S. Wiener, MD

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Review

This is an impressive prospective study, and the authors are to be congratulated for completing an all too rare multicenter, randomized, controlled trial in pediatric urology. One hundred patients with distal ureteral calculi aged 1-13 years matched for age, gender, and stone size were randomized to either shock wave lithotripsy (SWL) or transureteral lithotripsy (TUL). In the latter group, semirigid ureteroscopy with a 6 or 8.5 Fr scope was used to direct lithotripsy by holmium laser in 5 and pneumatic lithotripsy in 45 patients. Initial follow-up was by ultrasound at two weeks post-operatively. If stone-free, excretory urography was performed at 3 months; if residual stones were noted, “proper intervention” was performed. “Treatment was considered completely successful if there were no calculi on followup imaging.”

The results of this study appear valid. The study design was appropriate to examine differences in efficacy and complications between the two techniques. I will leave it to the statisticians to discuss whether the study was adequately powered to determine if any differences were significant. The two cohorts appear appropriately matched and essentially equivalent.

Lithotripsy techniques appear to be well-standardized between the six centers, although not identical. Both ultrasound and fluoroscopy were used to guide SWL using the same type of device at all centers, and there was the expected variation in the number of shocks and power delivered. The variation in TUL techniques is noted above. Appropriate follow-up imaging was performed, and a strict stone-free definition was used as the primary outcome. The descriptions of presentation and complications were thorough.

The study found that TUL was superior to SWL in terms of achieving the primary outcome of being stone-free. Stone-free rates were statistically significantly higher in the TUL group at discharge (not clear how this was determined), at two weeks, and overall at 3 months. The latter is the most important number with stone-free rates of 92% for TUL and 76% for SWL, regardless of number of sessions required. The efficiency quotient, a number used in the stone literature to compare the number of sessions required, was also statistically significantly superior for TUL (81%) vs. SWL (62%). Subject satisfaction was found to be 94% for TUL and 80% for SWL, but this may not be valid because the methodology of this determination was not presented.

Upon initial glance, the complication rate between cohorts appears similar; however, closer inspection does reveal one clinically important difference. Minor complications were similar except for expected differences such as skin bruising and steinstrasse for SWL and mucosal tearing for TUL. Concerning is the difference noted in major complications. Two ureteral perforations occurred in the TUL group (4% of total); one patient was managed with stenting, but the other required open surgical repair. These two significant complications were
associated with use of the larger 8.5 Fr ureteroscope which was employed “because of unexpected structural problems occurring with 2, 6 Fr devices.”

This well-designed study is applicable to urologists intervening for distal ureteral stones in children. The authors found TUL to be significantly more effective in achieving a stone-free outcome with a 16-22% difference compared to SWL at 2 weeks and 3 months. Repeat treatment rates were also significantly lower for TUL (18%) than SWL (38%). This is particularly important because children require general anesthesia for either modality. These numbers are very useful for counseling families when considering intervention. However, the superior stone-free rates for TUL come with a potential risk of significant ureteral injury. In this study, one patient did require open surgery as a consequence of ureteroscopic injury. Although this occurred in only 2% of subjects, the seriousness of this complication cannot be ignored when comparing to the completely non-invasive nature of SWL. The authors’ experience provided some caveats, albeit unproven, to the ureteroscopist. A smaller semi-rigid scope may be safer, as the two ureteral injuries occurred only with an 8.5 Fr scope. The authors did not tell us the age of the patients suffering injury, so it is unclear if patient size played a role in this complication. They also implied that laser TUL may be more effective than pneumatic TUL due to less retropulsion of stone fragments in proximally dilated ureters. Routine stenting of the ureter is likely not necessary, as the authors used stents in only 16% of TUL patients in cases with stone impaction or mucosal injury.

A number of minor concerns were mentioned but not well addressed in this study. The authors quoted an incidence of ureteral stricture of 1-4% after ureteroscopy in adults. They did not note ureteral strictures in any of the children, but follow-up was relatively short. Ureteral dilation was required in two patients to pass the 8.5 Fr ureteroscope; otherwise dilation was not necessary. Intentional ureteral dilation and, possibly, passive dilation with mere passage of the scope has been reported to cause vesicoureteral reflux. This was not examined in this report, but the authors suggest that secondary reflux is “generally temporary and low grade.”

In summary, this well-designed and well-conducted study demonstrates that TUL is superior to SWL in the management of distal ureteral calculi in children. It also reminds us that TUL can rarely result in significant ureteral injury. Patient safety, particularly in small children, must remain utmost in the urologist’s mind. Smaller ureteroscopes may be safer but, as the reviewer noted, they “demand expertise and experience to achieve superior results, whereas SWL is much simpler to execute.”