Clinical Trials of the Surgical Management of Urolithiasis: Current Status and Future Needs

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We reviewed the literature on the surgical treatment of urolithiasis. All prospective, randomized trials on the surgical treatment of stone disease were reviewed. Percutaneous nephrolithotomy (PNL) is superior to shockwave lithotripsy (SWL) or open surgery in the treatment of staghorn calculi. For ureteral stones, ureteroscopy appears to result in a higher stone-free rate and lower need for retreatment compared with SWL but has a higher complication rate and increased hospital stay. For lower pole renal calculi, PNL results in a higher stone-free rate and lower need for retreatment compared with SWL but has a higher complication rate and increased hospital stay. Most areas of surgical stone treatment have been addressed by a randomized controlled trial; however, most trials were of poor quality. Trials tend to focus only on radiologic outcomes. No study to date has been able to show a measurable quality of life benefit to patients, possibly because no condition-specific quality of life instruments have been developed. In addition, economic impact, both direct and indirect, has been rarely characterized. The surgical treatment of kidney stones is poorly researched. Future trials should be performed with adequate funding and patient-focused outcomes.

Index Words: Calculi; Randomized controlled trials; Percutaneous nephrolithotomy; Ureteroscopy; Shockwave lithotripsy

The surgical management of patients with kidney stones has undergone tremendous changes since the advent of shockwave lithotripsy (SWL), ureteroscopy (URS), and percutaneous nephrolithotomy (PNL). The rapid rate of change has brought tremendous benefits to patients in the form of less invasive options for kidney stone treatment, and, yet, it has also hindered the rigorous assessment of these techniques and technologies. Although surgical trials are difficult, especially in a rapidly advancing field, management of common urinary stone conditions remains controversial in large part because of the lack of good evidence. Thirty years on from the inception of minimally invasive stone treatment, most surgical treatment options have reached a degree of maturity that would allow for valid comparative trials, yet the literature on the subject is sparse.

This review sets out the evidence for the selection of treatment for the following conditions: (1) staghorn calculi; (2) renal calculi, including lower pole stones and SWL; and (3) ureteral calculi, including the choice of a ureteral stent. Proposals regarding the need for future trials will be made on the basis of the evidence available.

Staghorn Calculi

Meretyk et al[1] reported on a single-institution randomized controlled trial (RCT) for the treatment of staghorn calculi. A total of 50 patients were enrolled; 27 underwent SWL and 23 underwent PNL. They found that SWL monotherapy was inferior to the combination of PNL with or without adjunctive SWL. SWL monotherapy had a lower stone-free rate (22% *v* 74%) and a higher incidence of sepsis (37% *v* 9%).

Al-Kohlany et al[2] subsequently performed an RCT comparing open stone surgery with PNL in 79 patients with 88 staghorn calculi. They found that the stone-free rate was not significantly different (82% *v* 74%), but PNL was associated with significantly less intraoperative and postoperative complications, shorter hospitalization and procedural time, and earlier return to work. Thus, PNL with or without SWL can be considered the standard of care for the majority of patients harboring staghorn calculi.

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1548-5595/09/1601-0011$36.00/0

doi:10.1053/j.ackd.2008.10.011

Asymptomatic Renal Calculi

Do asymptomatic patients with renal calculi benefit from intervention in the form of SWL? Keeley et al[3] reported a trial of 228 patients randomized to SWL versus observation for renal calculi 5 to 15 mm in size and showed no benefit to treatment in terms of quality of life or stone-free rate. However, there was a benefit in terms of a reduced need for surgical intervention in the treated group after a mean follow-up of 2.2 years. Thus, SWL for the treatment of asymptomatic stones has some clinical benefits, but it has not been shown to result in improved stone-free rates. Further trials would be helpful to determine which, if any, asymptomatic patients benefit from SWL.

Lower Pole Renal Calculi

Renal calculi located in the lower pole calyces have been shown to have worse stone-free outcomes after SWL in retrospective case reports and, therefore, have been the subject of several studies by the Lower Pole Study Group. Albala et al[4] compared PNL with SWL for the treatment of patients with lower pole stones in 160 patients at 18 centers. A total of 128 patients completed the study, which clearly showed a higher stone-free rate with PNL. The benefit of PNL was magnified for stones greater than 10 mm in size. There were no differences in quality of life parameters using the Standard Form-36 questionnaire at 1 and 3 months. Although the complication rate was higher for PNL than SWL, the degree of these complications varied. Thus, the clinical significance of this difference was not fully explored in this study.

Pearle et al[5] reported a study comparing SWL with URS in patients with lower pole renal calculi $<$10 mm in size. The sample size calculation required 100 patients for 80% power to detect a 25% difference, but only 52 completed the study, despite recruitment from 19 hospitals over 3.5 years. The study was terminated early because of poor recruitment and lack of a difference between the groups. The stone-free rate for lower pole stones was slightly higher for URS (50%) than SWL (35%) as determined by a computed tomography scan at 3 months, but this did not reach statistical significance. Patients who underwent URS had more complications, required more pain relief, and took longer to return to normal activities. More patients reported that they would choose SWL again than patients who would choose URS.

Poor recruitment unfortunately limits the validity of some of the outcomes; nevertheless, the results challenge the assertion made in many single-center case series that URS is a treatment associated with a high success rate and low morbidity. Computed tomography scans were used to determine stone-free status, which might explain the disparity regarding stone-free status with prior studies in which less sensitive imaging was used. In addition, better ureteroscopic equipment is now available that could improve stone-free rates with this approach.

The Lower Pole Study Group has also compared URS versus PNL in patients with lower pole stones between 11 and 25 mm in size. The sample size was determined to be 80, but only 36 completed the protocol. Leveillie et al[6] found that PNL resulted in a higher stone-free rate (71% *v* 37%) and a reduced need for secondary procedures but had a higher postoperative complication rate. Patients reported similar quality of life outcomes. When asked if they would undergo the procedure again, 91% of PNL patients said they would compared with 69% of URS patients. Again, despite the poor recruitment in this study, the results are compelling in that they suggested that patients would prefer not to undergo URS, despite what many urologists might think.

Taken as a whole, the Lower Pole Group studies clearly show the limitations of prospective randomized studies in the surgical management of stone disease because of poor recruitment. Possible reasons for this include the following: lack of buy-in from investigators and patients, attempts to perform the trial in an inappropriate setting (ie, tertiary care), and lack of funding. These trials were largely unfunded, relying on the enthusiasm of participating surgeons to complete the studies. Surgical trials require surgeons and patients to forego making a treatment decision, yet patients typically are referred to surgeons on the assumption that a definitive