Impact of Stone Removal on Renal Function: A Review

Kyle Wood, MD, Tristan Keys, MD, Patrick Mufarrij, MD, Dean G. Assimos, MD

Wake Forest University School of Medicine, Winston-Salem, NC

Stone removal can improve renal function by eradicating obstruction and, in certain cases, an underlying infection. Stone-removing procedures, however, may negatively impact functional integrity. Many things may impact the latter, including the procedures used, the methods of assessing function, the time when these assessments are made, the occurrence of complications, the baseline condition of the kidney, and patient-related factors. In the majority of cases, little significant functional impairment occurs. However, there are gaps in our knowledge of this subject, including the cumulative effects of multiple procedures violating the renal parenchyma and long-term functional outcomes.

[Rev Urol. *2011;13(2):73-89 doi: 10.3909/riu0515*]

Key words: Renal function • Kidney stones • Shock wave lithotripsy • Percutaneous nephrolithotomy • Ureteroscopy

The majority of patients with symptomatic kidney stones pass them spontaneously. Those who are not able to do so may be subjected to a number of stone-removing procedures, most commonly, shock wave lithotripsy (SWL) and ureteroscopy. Percutaneous nephrostolithotomy (PCNL) is used to treat patients with large stones, those failing the aforementioned procedures, and those having certain renal and ureteral anatomic abnormalities. A small minority of patients may require laparoscopic, robot-assisted, or open surgical stone removal. A stone obstructing the kidney causes renal dysfunction that typically improves or resolves upon removal. However, stone-removing procedures may have a negative impact on renal function through direct or indirect mechanisms. We review the effects of different stone-removing procedures on renal function (Table 1). Both clinical series and experiments using animal models are analyzed in this article.

Table 1
Parameters Used to Measure Renal Function[a]

Morphologic/Histological	
Removal and evaluation of organ/tissue (animal studies)	
Imaging studies: MRI, CT, US (human studies)	
Functional	
Serum creatinine	
Estimated GFR	
Renal scintigraphy	
Renal plasma flow	
GFR	
Resistive indices	
Urinary Enzymes	

[a] These parameters are used to evaluate the effects of each treatment modality. Studies have been performed in both animals and humans.

CT, computed tomography; GFR, glomerular filtration rate; MRI, magnetic resonance imaging; US, ultrasound.

Shock Wave Lithotripsy

SWL was introduced in 1980 as a minimally invasive treatment for patients with upper urinary tract stones.[1] The majority of patients with renal calculi less than 2 cm are treated with SWL. Since its inception, studies have demonstrated its effectiveness and safety. Comminution of the calculus by SWL is due to mechanical forces generated by the shock waves. These mechanical forces are not innocuous and may result in renal parenchymal damage and vascular injury.[2] Whether the induced damage materializes into measurable short- and/or long-term bioeffects has been questioned.

Stone fragmentation is due to a number of mechanisms including spall fracture, circumferential compression, shear stress, and cavitation. Spall fractures result from the tensile forces of reflecting shock waves within the stone. Eventually these spall fractures coalesce and result in the destruction of the stone. Compression occurs because shock waves travel faster in the surrounding urine than within the stone, thus creating tensile stress that compresses the stone. Shock waves traveling through stones can cause shear stress, and amplification of these shock waves by reflection can result in both tensile and shear forces. The initial pressure waveform is positive and a negative phase follows. During the latter, cavitation bubbles are generated that subsequently enlarge and collapse. The cavitation bubbles generate their own shock waves that impart shear and tensile stress on the stones.[3] Formation of microjets from these cavitation bubbles has been demonstrated and serves as another means for stone destruction.[4] Coleman and colleagues demonstrated that cavitation bubbles were able to puncture through aluminum foil and even deform metal plates.[5] These cavitation bubbles are not only capable of destroying stones, but can also damage blood vessels and tissue. In another study, Bailey and associates detected cavitation within the tissue of a porcine kidney during SWL with a Dornier HM3 lithotripter.[6] Using high-speed photomicrography and ex vivo blood vessels from rat mesenteries, Chen and colleagues demonstrated that shock waves create cavitation bubbles that can result in vessel injury.[7] By modifying the waveforms produced by shock wave, Evan and associates were able to eliminate the creation of cavitation bubbles and, in the porcine kidney model, demonstrated diminished morphologic and functional changes.[8] These studies illustrate the prominent role cavitation plays in parenchymal and vascular injury following SWL.

SWL was introduced in 1980 as a minimally invasive treatment for patients with upper urinary tract stones. The majority of patients with renal calculi less than 2 cm are treated with SWL. Since its inception, studies have demonstrated its effectiveness and safety.

Animal Studies

Animal models have demonstrated both histologic and functional changes after SWL. Using canine and rabbit models, acute histologic damage to the renal parenchyma, renal vasculature, and the nephron structure has been noted.[9,10] Renal morphologic changes after shock waves include the development of subcapsular hematomas and focal parenchymal damage.[11] Light and electron microscopy of canine kidneys exposed to SWL demonstrated endothelial cell damage in small- to medium-sized arteries, veins, and capillaries. The parenchymal injury corresponded to the area where shock wave energy is emitted[9,12]; however, the consequences may be diffuse, as evidenced in swine models where free radical production occurs throughout the treated kidney.[13] Furthermore, chronic histologic changes of nephron loss and fibrosis within the cortex and medulla have been demonstrated in canine models.[14]

SWL treatment parameters, the presence of preexisting conditions, and the intrinsic characteristics of the kidney are important determinants of the extent of renal damage. Using a porcine model, Willis and colleagues reported that the volume of renal damage was less than 1% with 1000 shocks and 13.6% with 8000 shocks.[15] Connors and associates demonstrated that SWL-induced lesions in porcine models increased significantly in size as shock wave energy was increased from 12 to 24 kV.[16] Delius and colleagues demonstrated that kidney injury was dependent on the rate of shock wave administration. They compared 100 shocks/s to 1 shock/s in a canine model and assessed the extent of parenchymal injury, with damage in the former being more extensive.[17] Host factors such as the presence of pyelonephritis and renal immaturity have also been shown to augment the extent of renal injury in animal models (Table 2).[18,19]

SWL may impact certain renal functional parameters. An acute reduction in renal plasma flow (RPF) and glomerular filtration rate (GFR) of the treated renal unit has been demonstrated in the porcine model up to 4 hours after SWL. Interestingly, there is also a transient decrease in RPF with no effect on GFR of the untreated kidney at 4 hours after SWL. Renal plasma flow and GFR returned to baseline in the treated kidney and RPF returned to baseline in the untreated kidney within 24 hours after SWL.[16,19,20] Connors and colleagues demonstrated the important role that renal nerves play in modulating vascular responses in a porcine model. Renal plasma flow was significantly reduced up to 4 hours in the shocked kidney and its unshocked mate when renal nerves were intact, but only in the shocked kidney and not in its unshocked mate in the presence of denervation.[21]

Table 2
Determinants of the Extent of Renal Damage During Shock Wave Lithotripsy

Aggravating Factors
Increasing number of shocks
Increasing shock wave energy
Increasing the rate of shock wave administration
Host factors (pyelonephritis, renal immaturity)

There is some evidence suggesting a greater effect of SWL on the immature kidney. Using renin production as a marker of renal injury, Neal and associates demonstrated that the infant rhesus monkey, as compared with the adult, had persistent renin elevation. In the infant monkeys, renin remained elevated for more than 6 months, whereas in the adults levels returned to baseline within 3 weeks.[22] Handa and colleagues demonstrated that SWL-induced impairment of renal function was markedly greater in small immature porcine kidneys compared with larger mature porcine kidneys.[23] A greater reduction in RPF of both the shocked and untreated kidney was observed in the immature kidney group compared with the mature kidney group during the 4-hour posttreatment interval when this was measured. This difference was attributed to the fixed size of the focal energy zone impacting a larger percentage of the renal parenchyma of a smaller kidney.

Kaji and associates performed a left nephrectomy on 7-week-old rabbits. The remaining kidney then received varying levels of SWL. At 16 weeks, the rabbits demonstrated no significant change in animal growth, renal growth, or renal function. However, the post-SWL rabbits did have a significant increase in mean arterial pressure compared with the control rabbits. Histologic changes included thickening, fibrosis, and atrophy of the renal parenchyma proportional to the number of shock waves delivered.[24] Claro and colleagues exposed the kidneys of 40-day-old Wistar rats to varying amounts of shock wave energy. In all groups, there was no effect on animal or renal growth (Table 3).[25]

Human Studies

The literature on SWL tissue effects in human kidneys is more limited. SWL has been reported to cause renal and perirenal hematomas in humans. Although symptomatic renal and perirenal hematomas are quite rare, 0.6% to 1.3%, magnetic resonance imaging (MRI) and computed tomography (CT) have demonstrated that subclinical hematomas occur in as many as 25% of patients.[26-29] Increasing age is a risk factor for hematoma formation following SWL.[29] Krishnamurthi and Streem followed 19 patients with 21 SWL-induced hematomas for a mean of 19.6 months. Radiographic resolution of the hematoma occurred in 85.7% with the other hematomas decreasing in size or remaining unchanged. Patients did not experience new onset hypertension, worsening of preexisting hypertension, or increase in serum creatinine.[30] However, there have been case reports of large post-SWL hematomas resulting in renal failure,[31] blood transfusion,[32] and prolonged hospitalization. Fortunately, such occurrences are rare, but they clearly demonstrate the renal destructive potential of SWL.

Investigators have studied the impact of SWL on the kidney with various imaging modalities. Kaude and

Table 3
Animal Model Studies Have Demonstrated Histologic and Functional Damage

Shock Wave Lithotripsy	
Animal Models	
Histological Damage	**Functional Damage**
Parenchyma	Renal plasma flow
Nephron	Glomerular filtration rate
Vasculature	Serum creatinine
Histology	
Acute Changes	**Chronic Changes**
Parenchymal hemorrhage	Nephron loss
Damage to small veins and arteries	Cortical fibrosis
Glomerular and peritubular capillaries	Medullary fibrosis
Cellular and tubular necrosis	

colleagues studied the acute effects of SWL on morphology and function of the kidney by intravenous pyelography (IVP), quantitative radionuclide renography, and MRI.[26] Excretory urograms demonstrated an enlarged kidney in 18% of cases and partial or complete obstruction of the ureter by stone fragments in 37% of cases. Quantitative radionuclide renography images showed partial parenchymal obstruction in 25% of treated kidneys and total parenchymal obstruction in 22%. MRI disclosed one or more of the following abnormalities in 63% of treated kidneys: loss of corticomedullary differentiation, perirenal fluid, subcapsular hematoma, hemorrhage into a renal cyst, and/or miscellaneous abnormalities. Posttreatment abnormalities developed in 74% of targeted kidneys based on one or more of the aforementioned tests. Dumont and associates corroborated this result by demonstrating a reduction in dimercaptosuccinic acid (DMSA) uptake by SWL-treated kidneys in 59% of patients after 48 hours.[33]

Studies measuring urinary enzymes and other markers of renal injury in those treated with SWL have shown that there are transient elevations in the excretion of these substances that usually return to baseline in a matter of days to weeks after treatment.[34-36] Assimos and colleagues demonstrated transient post-SWL increases in *N*-acetyl-β-glucosaminidase (NAG) and β-galactosidase in urine with return to baseline levels by 28 days.[34] Lambert and associates evaluated the effects of escalating versus fixed voltage SWL, and demonstrated that the urinary excretion of β2 microglobulin and microalbumin, an index of renal injury, was higher 1 week posttreatment when the latter method was used.[37] Animal model studies have demonstrated the positive correlation of histologic renal tubular damage and urinary enzyme excretion generated by shock wave energy, supporting the validity of this approach for monitoring renal injury.[38]

Some investigators have measured urinary enzyme excretion and parameters of renal function before and after SWL. Rutz-Danielczak and associates reported that urinary enzyme excretion increased in conjunction with a reduction of GFR and RPF immediately after SWL, with all parameters returning to baseline within days to months.[36] Jung and associates reported that elevations in the excretion of urinary enzymes including alanine aminopeptidase, alkaline phosphatase, γ-glutamyl-transferase, and NAG did not uniformly correlate with reduction in renal function as evaluated with ^{99m}Tc-diethylenetriamine-pentaacetic acid (DTPA) isotope clearance.[39]

Eterović and colleagues compared SWL to pyelolithotomy and observed that SWL resulted in decreased RPF in both the treated and untreated kidney for up to 90 days.[40] These results are similar to those observed in the porcine model by Connors and associates, suggesting that the renal nerves may play a pivotal role in renal vascular tone not just in pigs but perhaps in humans as well.

Staged SWL has been used to manage patients with bilateral renal calculi instead of synchronous bilateral SWL due to concerns about bilateral obstruction and possible renal failure. Some investigators, however, have demonstrated that bilateral SWL does not result in worsening renal function using serum creatinine as a marker, which admittedly has some limitations.

Staged SWL has been used to manage patients with bilateral renal calculi instead of synchronous bilateral SWL due to concerns about bilateral obstruction and possible renal failure. Some investigators, however, have demonstrated that bilateral SWL does not result in worsening renal function using serum creatinine as a marker, which admittedly has some limitations. Pienkny and Streem reported no significant increases in serum creatinine in patients undergoing bilateral SWL at a mean follow-up of 3.5 years.[41] Perry and associates retrospectively evaluated the records of 120 patients who received synchronous bilateral SWL. There were no cases of bilateral obstruction, renal failure, or deterioration of renal function at an average of 21-month follow-up.[42]

Solitary Kidney and Renal Insufficiency

There is concern that SWL may be more detrimental to the solitary kidney or to patients with underlying renal insufficiency because there is less functional reserve. Long-term effects of SWL have been conflicting with some groups demonstrating no change in renal function and others demonstrating significant differences. Karlsen and colleagues reported a significant decrease in inulin clearance and an increase in urinary β2 microglobulin excretion 24 and 48 hours after treatment of patients harboring calculi in solitary kidneys while serum creatinine remained unchanged.[43] Kulb and associates found no significant changes in serum creatinine or RPF 3 months post-SWL of solitary kidneys.[44] In addition, Zanetti and associates reported no long-term changes of serum creatinine at follow-ups ranging between 24 and 56 months.[45] Cass demonstrated no decrease in GFR in the solitary kidney 24 months after SWL.[46] Limited information exists on the impact of SWL in patients with chronic kidney disease. Chandhoke and associates reported on the long-term effects of SWL on renal function in patients with chronic renal insufficiency (CRI) and/or solitary kidney (mean follow-up, 41.5 months). They considered a change of 20% or greater in the GFR as significant deterioration or improvement in renal function. Renal function deteriorated in 22% of patients with a solitary kidney and creatinine of less than 2 mg/dL. All patients with a creatinine between 2 and 3 mg/dL demonstrated long-term improvement of renal function. All patients with creatinine greater than 3 mg/dL undergoing SWL had short-term improvement but eventual long-term deterioration of renal function, with the majority requiring dialysis within 2 years.[47] This suggests that patients with solitary kidneys or those with mild or moderate renal insufficiency will not experience renal functional deterioration after SWL and, in fact, may experience benefits, possibly due to relief of obstruction. Patients with more profound renal insufficiency typically progress to dialysis dependency that may be a result of the natural history of their renal disease.

One of the factors that must be considered in determining the actual impact of SWL on renal function is the potential for improvement with relief of obstruction. This was demonstrated in a study reported by Paryani and Ather of 13 patients with renal insufficiency (serum creatinine $>$ 2.0 mg/dL) harboring obstructing stones. Serum creatinine was 5.1 mg/dL at the time of presentation, 2.1 mg/dL after draining the affected renal unit(s) with an internalized stent or percutaneous nephrostomy, and 1.8 mg/dL after SWL.[48]

Children

Because the kidneys of children are still developing, there has been concern that SWL may impair renal growth and impact kidney function. Lottmann and associates evaluated 15 children receiving SWL with DMSA renal scans 24 hours before SWL and at 6 months or longer after treatment. The DMSA renal scans demonstrated no impairment at follow-up.[49] Picramenos and colleagues evaluated 50 children with DMSA scans immediately before, at 1 month, and 3 months after SWL and reported no decreases in renal function at these intervals.[50] Furthermore, a prospective study of children under age 2 years receiving SWL demonstrated no parenchymal damage or reductions in renal function as assessed by renal scintigraphy at 6 months posttreatment and by renal ultrasonography at a mean of 36 months follow-up.[51] Similar findings were reported by Wadhwa and associates, who demonstrated no functional changes at 6 months after SWL as measured by DMSA and ^{99m}Tc-ethylene dicystine (EDC) scintigraphy.[52] Fayad and colleagues prospectively studied renal function in 100 children treated with SWL. DMSA and DTPA scans 6 months postoperatively did not demonstrate any parenchymal scarring or change in GFR compared with preoperative evaluation.[53] Other long-term studies (mean, 31.7-month follow-up) using renal scintigraphy demonstrated no effect on GFR.[54] Many other investigators have reported on the safety of SWL in this young cohort.[54-61]

A small number of investigators have reported that SWL in children may have either an acute impact or chronic effects on renal function. A significant elevation in the urinary excretion of aspartate transaminase, alkaline phosphatase, lactate dehydrogenase and β2 microglobulin was observed in children following SWL with return of levels to baseline within 2 weeks.[62] Reis and colleagues followed 18 children with preoperative and postoperative DMSA renal scintigraphy and other imaging studies. One patient (5%) experienced a

Table 4
The Effects of Shock Wave Lithotripsy in Children

Study	Measurement	Follow-Up (mo)	Adverse Effects
Fayad A et al (2010)[53]	DMSA, DTPA	6	None
Griffin SJ et al (2010)[61]	DMSA	6	None
Wadhwa P et al (2007)[52]	DMSA, EDC	6	None
Lottmann HB et al (2001)[60]	DMSA	6	None
Lottmann HB et al (2000)[51]	Ultrasound, DMSA	36	None
Lottmann HB et al (1998)[49]	DMSA	6	None
Picramenos D et al (1996)[50]	DMSA	3	None
Goel MC et al (1996)[54]	DTPA	31.7	None

Most studies have demonstrated no adverse effects
DMSA, dimercaptosuccinic acid; DTPA, ^{99m}Tc-diethylenetriaminepentaacetic acid; EDC, ^{99m}Tc-ethylene dicystine.

decrease in tubular function and an enlargement of the treated kidney at 6 months postoperatively; of note, the aforementioned patient received three sessions of SWL.[63] Lifshitz and associates retrospectively reviewed 29 pediatric patients treated with SWL with a 9-year mean follow-up. A disparity in renal growth between the treated and untreated kidneys was found, the former with growth retardation.[64] Although the alterations seen in renal growth may have been due to some intrinsic renal pathology, SWL could have played some role. The effects of SWL on children, especially those receiving multiple treatments, needs to be further assessed (Table 4).

Percutaneous Nephrolithotomy

Since the first documented utilization of a percutaneous method for treatment of renal calculi in the 1970s,[65] PCNL has proven to be an effective technique for managing appropriately selected patients with large, complex renal stones.[66,67] As the renal parenchyma is directly invaded with this approach, renal function may be impacted. In addition, if the collecting system and ureter are violated during this procedure, this may impair egress of urine from the kidney, resulting in functional compromise. However, many of these kidneys are obstructed before this procedure and stone removal via this technique may promote an improvement in function.

Animal Studies

Initial studies using animal models to evaluate renal injury incurred during percutaneous renal surgery focused primarily on the overall anatomic and functional changes. In one of the earliest investigations, Webb and Fitzpatrick assessed effects in 31 dogs, with 15 receiving a nephrostomy tract and 16 being subjected to PCNL of an implanted stone using electrohydraulic or ultrasonic lithotripsy.[68] They evaluated morphologic changes at 48 hours and 6 weeks with IVP, corrosion casts, and creatinine clearance. In both groups, they demonstrated that the nephrostomy tract showed edematous changes that resolved by 6 weeks with only a fine linear scar as a remnant. Creatinine clearances at baseline, 48 hours, or 6 weeks were similar. David and colleagues subjected swine to either insertion of a percutaneous nephrostomy tube (PCN) that was left indwelling for 3 weeks, open surgical pyelotomy, or delivery of extracorporeal shock wave energy to the kidney.[69] They found that total GFR measured with scintigraphic techniques acutely dropped in those undergoing nephrostomy or those exposed to shock wave energy. This reverted to normal at 7 days after the latter and 1 month after the percutaneous intervention. There were no such changes observed after pyelotomy. The animals were also evaluated with MRI 1 day, 7 days, and 4 weeks after these procedures. There was loss of corticomedullary differentiation at 1 day after treatment in those kidneys undergoing nephrostomy or exposed to shock wave energy that again reverted to normal at 7 days. The pyelotomy group was free of parenchymal changes. Another study comparing various renal interventions including PCN, SWL, pyelotomy, and open surgical nephrostomy in a porcine model showed that PCN caused the greatest amount of histologic renal damage (scar) at 1 month.[70] However, the extent of the latter was minimal: less than 2% of renal volume. Declines in renal function as measured by serum creatinine, creatinine clearance, or effective renal plasma flow did not occur with any of the aforementioned modalities.

Animal models have also been used extensively in studies comparing the effects of various methods of percutaneous tract dilation on renal morphology. In one of the earliest studies, Clayman and colleagues examined renal damage incurred during tract dilation, comparing balloon and sequential fascial dilating systems.[71] Using pigs, bilateral nephrostomy tracts were created, the right kidney being dilated to 24F with Amplatz semirigid fascial dilators, and the left kidney being dilated to 36F with a rapidly expanding balloon dilator. The dilators were left in place for 10 minutes before being removed, and the tract was closed. The remaining animals were killed at 6 weeks. Using Masson trichrome staining for collagen and photographic planimetry to calculate scarring of the renal parenchyma, the mean percentage of total cortical volume damaged was determined to be 0.13% in the right kidneys and 0.16% in the left kidneys. The method of dilation did not influence results, both yielding minimal histologic renal damage. In a more recent porcine study of these two dilating methods, Al-Kandari and associates established 30F tracts after which they left 20F Council catheters in the collecting system for 48 hours.[72] At 4 and 6 weeks, both methods yielded small scars. Traxer and colleagues compared a standard-sized tract to a smaller one in a porcine model.[73] Kidneys were either dilated to 28F with insertion of a 30F access sheath or to 11F with a similar-sized sheath; dwell times in either setting were 1 hour. The larger tract kidneys were drained with a 22F nephrostomy tube and an 8F device was used for the smaller tracts. These were each removed after 24 hours. At 6 weeks, the kidneys were harvested and sections were stained with Masson's trichrome stain. The degree of fibrosis was determined using photographic planimetry. The mean percentage of scarred renal parenchyma was 0.63% in the standard-sized tracts, and 0.91% in the miniature tracts, with no statistical difference. In a related canine study evaluating single versus multiple stepwise dilation, Travis and associates exposed the kidneys via open surgery and created a 24F nephrostomy tract using a single rigid dilator, sequential dilators, balloon dilation, or metal telescoping dilators.[74] A 25F access sheath was left in place for several minutes, and then the kidneys were either removed for immediate examination or re-evaluated at 48 hours or 6 weeks. Only specimens that were subjected to single rigid dilation were examined at all three intervals. No significant difference in gross or histologic renal morphology was found between methods immediately following tract dilation. IVP at 48 hours did not show any parenchymal damage, and only a fine linear scar was found at 6 weeks. Thus, animal models have demonstrated no significant chronic renal parenchymal damage with tract dilation.

Functional studies have also been undertaken in animal models. In a porcine model, unilateral nephrostomy tracts were established by Handa and colleagues and were dilated to 30F using both sequential and balloon techniques.[75] These experimental groups were compared with a control group of sham-accessed animals. GFR, RPF, and renal clearance of para-aminohippuric acid (EPAH) were measured at baseline, 1.5, and 4.5 hours after intervention; the kidneys were subsequently removed and inspected grossly and histologically. Creation of nephrostomy tracts by both methods significantly reduced GFR and RPF at 4.5 hours; no such response was seen in the controls. Interestingly, the untreated contralateral kidneys also had similar functional decreases (as seen in SWL). It was hypothesized that these responses were due to vasoconstriction induced in both treated and untreated kidneys. Histologic examination demonstrated areas of ischemia and trauma in the treated kidney up to 2.3 times greater than the size of the tract. These results suggest that renal parenchymal injury sustained during PCNL may be greater than previously reported. This group did other experiments where the period of observation was extended.[76] Balloon dilation was used for unilateral nephrostomy tract creation in swine. Renal functional parameters in both kidneys were measured at baseline and then at 1 hour and 72 hours after intervention. GFR and RPF in the treated renal unit were significantly lower, approximately 55% at 1 hour postintervention, but reverted to baseline at 72 hours. In contrast, EPAH remained significantly decreased at 72 hours in the treated kidneys. However, the functional decline in the contralateral kidney was not observed in this study.

Other experiments by this group assessed renal function immediately after simultaneous bilateral percutaneous access in pigs.[77] Renal functional parameters were measured at baseline, 1.5, and 4.5 hours postintervention. GFRs and RPF were reduced by 35% at 4.5 hours in both kidneys, which is comparable with reductions in renal function seen during unilateral PCN. The aforementioned studies consistently demonstrate that both GFR and RPF decline in the targeted kidney with PCN. These declines were shown to be transient when follow-up was extended to 72 hours. These investigators also showed that tubular dysfunction occurs and that its duration appears to be longer than 72 hours.

Human Studies

The impact of PCNL on renal function in human patients has been assessed with various methods. Serum and urine tests have been used. Handa and associates performed a retrospective analysis of 196 patients undergoing single-stage unilateral PCNL[75] where serum creatinine was measured before and 1 day after intervention. Overall, the entire group had a significant increase in concentration (0.14 $\pm$ 0.02 mg/dL; $P < .001$). Sixty-four percent had a significant increase (average, 0.26 $\pm$ 0.02 mg/dL), 19% remained unchanged, and 17% had a decrease. This group completed another retrospective analysis in which they evaluated 576 patients undergoing unilateral and bilateral PCNL, including procedures requiring single and multiple accesses.[77] In each group, they found that a majority of the patients had a significant increase in serum creatinine 1 day after intervention, with a greater increase found in the bilateral PCNL groups. In another study, Saxby assessed urinary creatinine clearance immediately before, 24 hours after, and 2 weeks after unilateral PCNL and noted no differences.[78] Urinary enzyme measurements have also been used to assess for renal injury after PCNL. Urivetsky and coworkers measured urinary lysozyme activity in a prospective study of 42 patients.[79] Urine samples were obtained at hospital admission, immediately after percutaneous access, and on postoperative days 1 and 3. The majority had normal urinary levels throughout the procedure and postoperatively. Five patients who had increased levels before intervention were found to have lower levels on day 3. Eight patients had an increase in levels at time of access that trended downward postoperatively. Trinchieri and colleagues similarly measured NAG in the urine excreted from the treated kidney 24 hours after PCNL in 11 patients and found no significant change compared with preoperative levels.[80] Saxby, in the same study just mentioned, measured urinary prostaglandin F2α immediately before and at 24 hours and 2 weeks after unilateral PCNL.[78] Urinary prostaglandin levels were increased at 24 hours, but returned to baseline levels at 2 weeks.

Renal function after PCNL has also been assessed using nuclear medicine techniques. Alken used ^{131}I-orthoiodohippurate scans in 12 patients undergoing PCNL, and found that 10 patients had a 10% improvement, whereas renal function declined 3% to 5% in the remaining 2 patients.[81] In a retrospective study by Marberger and associates, split ^{131}I-orthoiodohippurate renograms were performed preoperatively in 18 patients who underwent PCNL and postoperatively between 12 and 43 months after intervention.[82] Renal function increased 7.6% ± 2.8% overall; however, the researchers attributed this to removal of the obstructing calculi. In a prospective series of 11 patients, Ekelund and associates performed renal scintigraphy using ^{99m}Tc-DTPA to evaluate overall renal function after unilateral PCNL.[83] In these patients, who had nonobstructing and noninfectious stones, there was a moderate decrease in renal function 1 day postoperatively that returned to near baseline values at 14 days. However, in three patients, there was a 20% decrease in renal function of the treated kidney at 14 days. Similar results were reported by Schiff and associates who prospectively evaluated 33 patients with nonobstructing calculi undergoing unilateral PCNL.[84] Follow-up with renal scintigraphy using ^{99m}Tc-DTPA was between 3 to 12 months. They found no significant functional change in the group overall. However, subgroup analysis showed a non–statistically significant drop in renal function (−3.38%) in patients examined less than 90 days after intervention. In contrast, there was a nonsignificant increase in function (0.67%) in patients examined at greater than 90 days. Additionally, in patients who sustained an intraoperative complication, renal function decreased significantly (−13.17%). Another report analyzed the effect of PCNL on regional function of the kidney.[85] Researchers found no significant difference in the uptake of ^{99m}Tc-DTPA in the portions of the kidney containing nephrostomy tracts. Mayo and associates performed a prospective study of 15 patients using pre- and postoperative 24-hour creatinine clearance and ^{99m}Tc- DMSA to estimate each kidney's GFR.[86] They found no significant change in renal function in those patients with noninfectious stones. They did show, however, a significant increase in renal function in those patients who had infected stones. Al-Kohlany and colleagues randomized 79 patients with complete staghorn calculi to either PCNL or open surgery.[87] Utilizing ^{99m}Tc-mercaptoacetyltriglycine (MAG3) to calculate split GFR of the treated kidney between 3 and 14 months after intervention, they found that renal function in 91% of the PCNL group either improved or remained stable. Chatham and associates also performed a prospective study of 19 patients using MAG3 scintigraphy to evaluate renal function.[88] They observed an overall increase in the contribution of the targeted kidney to global renal function for the entire group (36.8% preoperatively and 38.5% postoperatively), with renal function preserved or improved in 16 patients (84%). A total of 7 patients (37%) had an overall improvement in function, whereas there were only 3 patients (16%) who had a decrease in renal function. Moskovitz and associates used quantitative single-photon emission CT (SPECT) measurement of ^{99m}Tc-DMSA uptake by the kidneys in 88 patients undergoing unilateral PCNL for treatment of staghorn calculi.[89] At follow-up between 2 and 24 months, they demonstrated no significant difference between preoperative and postoperative percent uptake of ^{99m}Tc-DMSA (11.9% ± 5% vs 11.6% ± 5%, respectively) despite there being a significant decrease in the total functional volume of the treated kidney (235 cc ± 62 cc to 224 cc ± 59 cc).

Additionally, there was a significant decrease in the functional volume of the surgically treated poles from 91 cc ± 30 cc to 82 cc ± 27 cc, although there was no difference in regional uptake of ^{99m}Tc-DMSA. They did not observe any change in the functional status of the contralateral kidney. In another study utilizing SPECT with ^{99m}Tc-DMSA, Ünsal and colleagues randomized 50 patients to balloon, metal, or Amplatz dilation to evaluate each modality's effect on renal function.[90] Follow-up was 3 to 6 months after intervention. They reported no significant difference between treatment groups. Total relative uptake of the treated kidney was preserved in 74% of patients, increasing from 42.2% to 44.1% overall. Sixteen percent of patients had an improvement in renal function, whereas 10% experienced a decline. Also, out of nine new focal cortical defects noted postoperatively, there were six that corresponded to the access site.

Color Doppler ultrasonography (CDUS) has been used to explore the effect of PCNL on renal morphology in humans. Kiliç and associates retrospectively selected 41 patients who had undergone unilateral single access PCNL and performed follow-up studies between 30 and 58 months after intervention.[91] They measured vascular resistive indices (RI) and parenchymal thickness. The postoperative parenchymal thickness of the treated kidney was significantly decreased, and RI was significantly increased. This group also performed a prospective study of 24 patients using CDUS that was completed before and at 1 day, 3 months, 6 months, and 12 months following PCNL.[92] They found that the RI significantly increased in the nonaccessed pole of the treated kidney but not in any of the other poles.

Multiple Tracts

More than one access tract may be required in certain patients with significant stone burden. In such cases, there is increasing risk of parenchymal injury with additional tracts, and the cumulative effect could potentially lead to acute or chronic renal functional impairment. The impact of multiple tracts on renal function has been investigated in both animal and human studies, and the results are divergent. Handa and colleagues compared single- versus multiple-tract (3) access in a porcine model.[93] GFR and RPF were measured immediately before and at 1.5 and 4.5 hours after intervention. In both single- and multiple-tract access groups, GFR and RPF declined significantly in both the treated and untreated renal units, although there were no significant differences between single- and multiple-tract cohorts. This group also performed a retrospective analysis of 33 patients undergoing either single- or double-tract access, assessing serum creatinine and estimated GFR preoperatively and at 24 and 48 hours after PCNL. In both groups, similar elevations in creatinine concentrations and decreases in GFR were noted at 24 and 48 hours as compared with preoperative baseline levels. In a similar retrospective study, pre- and postoperative creatinine concentrations were examined in 576 patients undergoing unilateral or bilateral single- or multiple-access PCNL.[77] There was an acute rise in creatinine levels in all groups, and the reduction in renal function was independent of the number of access tracts. Hegarty and Desai retrospectively compared preoperative and postoperative serum creatinine and creatinine clearance in 40 patients undergoing single-tract PCNL or multiple-tract PCNL (range, 2 to 6 tracts).[94] The multiple-tract cohort experienced a significant increase in serum creatinine and decrease in creatinine clearance, whereas, in contrast to the previous studies, there was no change in the single-tract cohort.

More than one access tract may be required in certain patients with significant stone burden. In such cases, there is increasing risk of parenchymal injury with additional tracts, and the cumulative effect could potentially lead to acute or chronic renal functional impairment.

Solitary Kidney and Renal Insufficiency

There is limited information on the impact of PCNL in patients with solitary kidney or those with renal insufficiency. There is significant overlap in some of these studies, with some patients having both conditions. Segura and colleagues reported no detectable compromise in renal function in 15 patients with solitary kidneys immediately after PCNL.[95] In a retrospective study of 53 patients with solitary kidneys, Jones and associates demonstrated stable serum creatinine

There is limited information on the impact of PCNL in patients with solitary kidney or those with renal insufficiency. There is significant overlap in some of these studies, with some patients having both conditions.

and overall preservation of renal function immediately after PCNL, even though 26% of patients had impaired preoperative renal function.[96] Streem and colleagues similarly noted stable or improved serum creatinine 1 month after PCNL in five patients.[97] Furthermore, Liou and Streem reported no significant long-term postoperative change in serum creatinine or estimated GFR in 18 patients with solitary kidney at a mean follow-up of 68 months.[98] They did demonstrate a significant positive correlation between pretreatment serum creatinine with the subsequent increase in GFR for patients with renal insufficiency. Canes and associates used a prospective database with retrospective chart review to assess postoperative renal function in 81 patients with solitary kidneys undergoing percutaneous renal surgery.[99] They used the modification of diet in renal disease (MDRD) estimated GFR to determine renal function immediately before surgery and at 1 day, 1 month, and 1 year after intervention. Even though 76% of patients had baseline stage 3 or higher chronic kidney disease (CKD), GFR was unchanged at day 1, and significantly improved at 1 month and 1 year. Moreover, 37% of patients improved their CKD class, 56% remained stable, and only 7% had worsened 1 year after intervention.

In another long-term study, though, Chandhoke and associates found that between 36 and 65 months after PCNL of a solitary kidney, two out of seven patients had a significant deterioration in GFR, one patient had a significant increase, and four patients had preservation of GFR.[47] Agrawal and colleagues performed a retrospective study of 75 patients with severe renal functional impairment (mean serum creatinine of 7.5 mg/100 mL).[100] Thirty-two patients had a solitary functioning kidney. Preoperative serum creatinine was compared with levels after renal drainage with PCN and also after subsequent stone removal via PCNL at 2.5- to 9-year follow-up. Overall, the average serum creatinine decreased significantly to 3.01 mg/dL at final follow-up. Sixty-four patients had an improvement in function, whereas 11 patients had stable or declining function. Interestingly, in 50 patients initially treated by PCN, the authors report that renal function increased with decompression and further improved with subsequent stone removal. In another long-term follow-up study, Kuzgunbay and associates retrospectively analyzed data from 16 patients with renal insufficiency (creatinine $>$ 1.4 mg/dL); minimum follow-up of 39 months.[101] Overall postoperative creatinine was not significantly different; although levels returned to normal in six patients, it remained stable in six patients and increased in four patients. Yaycioglu and colleagues compared a group of 19 patients with impaired renal function (serum creatinine $>$ 1.5 mg/dL) with patients with normal renal function undergoing PCNL.[102] At an average follow-up of 15.6 months, there was no significant change in renal function as determined by serum creatinine in either group. Chandhoke and associates evaluated three patients with moderate renal insufficiency (serum creatinine 2 to 3 mg/dL) undergoing PCNL, and found that two had preserved GFR, whereas one had significantly improved GFR at long-term follow-up between 24 and 60 months.[47] GFR also improved significantly in one patient with severe renal insufficiency (serum creatinine $>$ 3 mg/dL).

Bilen and colleagues used the MDRD estimated GFR to evaluate short-term renal functional changes in 185 patients classified according to the K/DOQI CKD system.[103] Baseline for all patients was CKD Stage 3 or higher. At patient discharge, there was a significant increase in GFR for patients in each stage. Three months after intervention, the overall preoperative GFR significantly increased from 42.4 mL/min/1.73 m^2 to 48.4 mL/min/1.73 m^2. They did note, however, that renal function improvement was more likely to be found in patients who had a higher CKD stage than in patients with lower stage disease. Kukreja and associates retrospectively studied 84 patients with various degrees of renal insufficiency, evaluating serum creatinine after intervention (of 96 renal units, 87 PCNL, 7 open surgical nephrolithotomy, and 2 nephrectomy).[104] Overall, 67.9% of patients had improvement or stabilization of their renal function at an average follow-up of 2.2 years. In contrast to other studies, however, they reported that patients with more severe CKD were at risk for developing end-stage renal disease. Only 1 out of 13 patients (7.7%) with serum creatinine $<$ 2 mg/dL had decline in renal function, whereas 11 of 43 (25.6%) with a serum creatinine of 2.0 to 2.9 mg/dL, and 10 of 23 (43.5%) with a serum creatinine of 3.0 to 5.9 mg/dL sustained reductions in renal function. All five patients with serum creatinine $>$ 6 mg/dL progressed to ESRD. Additionally, they found that in 12 patients with solitary kidneys, 6 experienced worsening renal function. In summary, for patients with a solitary kidney, renal insufficiency, or both, a majority of the literature indicates that there is no significant impairment of renal function after PCNL. This trend may be due to relief of underlying obstruction.

Pediatrics

There are limited studies evaluating the impact of PCNL on renal function and morphology in the pediatric patient population. In a prospective study looking at short-term outcomes, Wadhwa and associates performed

^{99m}Tc-DMSA scintigraphy, split function ^{99m}Tc-EDC scans, and calculated GFR using ^{99m}Tc-DTPA in nine pediatric renal units.[52] At 3 months after PCNL, there was no overall change in GFR as compared with preoperative levels. No new cortical scars were observed on DMSA scintigraphy, and there was no significant change in split function EDC scans. In patients aged less than 5 years, Mahmud and Zaidi demonstrated no scarring as assessed with ^{99m}Tc-DMSA scans in 17 kidneys 4 to 6 weeks after PCNL. The lack of such preoperative imaging did not permit functional comparisons.[105]

Desai and associates retrospectively analyzed data from 56 patients less than age 15 years subjected to PCNL, and at 3 to 6 months after PCNL, they report preserved function in 36 renal units based on a weak index of function, IVP.[106] ^{99m}Tc-DMSA scintigraphy performed in six children both pre- and postoperatively showed no new scar formation. Additionally, 53 patients had no change in serum creatinine 1 year after intervention. Samad and colleagues prospectively studied 56 children with postoperative ^{99m}Tc-DMSA to evaluate for renal parenchymal damage at a mean follow-up of 3.6 months after PCNL.[107] New cortical defects were detected at the access sites in only 5% of patients. In the four patients who had both pre- and postoperative scans, no decline in ipsilateral renal function was detected. Mor and associates evaluated 10 children with renal scintigraphic studies (either DMSA, DTPA, or MAG3) before and at a mean follow-up of 23 months after PCNL.[108] Renal functional deterioration was only detected in one patient, who had previously been subjected to two such operations. Dawaba and colleagues prospectively studied renal function in 65 children treated with PCNL using ^{99m}Tc-DTPA to calculate GFR and ^{99m}Tc-DMSA to evaluate for renal scarring.[109] At a mean follow-up of 40 months, no significant cortical scarring was observed, and the mean GFR significantly increased from 28.8 ± 1.2 mL/min to 36.1 ± 9.9 mL/min in the treated renal unit. Only four patients had a decline in GFR. Collectively, these studies suggest that the risk of clinically significant renal functional decline in pediatric patients subjected to PCNL is small.

Open Surgery

Open surgical stone removal is rarely performed in today's practice.[110] There are, however, some patients with extremely complex staghorn stones, those with coexistent abnormalities of the collecting system or ureter, and those who have failed minimally invasive approaches who may require this approach. The majority of information on renal functional outcomes pertains to anatrophic nephrolithotomy (ANL). The classic method of this procedure involved the following steps: isolation and occlusion of the posterior segmental renal artery, intravenous injection of methylene blue to define the anatrophic demarcation, occlusion of the main renal artery and establishment of hypothermic ischemia, nephrotomy along the anatrophic demarcation, stone removal, reconstruction of the collecting system, and closure of the renal capsule. Modifications of this approach have also been described.

Thomas and colleagues reported a 30% reduction in function of the operated kidney as assessed by ^{131}I hippuran scanning in 13 patients subjected to classic ANL at a mean of 13.6 months after surgery. Nonetheless, they did note that the contralateral kidney had a 13% increase in function at this interval; the total effective renal plasma flow was decreased by 8%.[111] Stubbs and associates evaluated serum creatinine levels and creatinine clearance in patients with solitary kidneys subjected to classic ANL. Preoperative serum creatinine was 1.6 mg/dL and postoperatively it remained the same (average follow-up of 6 years). Creatinine clearance rose slightly from 52 to 55 cc/min.[112] Demler and colleagues demonstrated the feasibility of performing a simultaneous classic bilateral ANL on 14 patients. Serum creatinine levels peaked 2 to 3 days postoperatively with steady return to preoperative baseline.[113] Gough and Baillie evaluated the effects of classic ANL on renal function in nine children prospectively. Seven children experienced a significant reduction, ranging from 6% to 16%, in renal function as measured by DMSA scintigraphy that was performed at least 4 months postoperatively.[114]

A number of investigators have described their results with a modified ANL in which a nephrotomy is performed without defining the intersegmental plane; some of these reports made comparisons between the approaches. Kijvikai and colleagues reported on renal functional outcomes achieved with the classic and modified ANL as assessed by DTPA renal scans preoperatively and at 6 weeks postoperatively. The median percentage reduction of GFR in the operated kidney of patients undergoing classic

Open surgical stone removal is rarely performed in today's practice. There are, however, some patients with extremely complex staghorn stones, those with coexistent abnormalities of the collecting system or ureter, and those who have failed minimally invasive approaches who may require this approach.

ANL was 9.13, whereas it was 27.25 in the patients undergoing a modified procedure. This suggests that the modified ANL resulted in more acute renal parenchymal damage.[115] Ramakrishnan and associates reported on 26 patients subjected to a similar modified procedure; renal function assessed by DMSA scans remained stable in 55%, improved in 32%, and worsened in 13% at 6 months postoperatively.[116] Morey and associates demonstrated only a 4% postoperative decrease in ipsilateral renal function assessed by DMSA scans in 15 patients who underwent a modified ANL.[117] Belis and colleagues evaluated 13 patients subjected to modified ANL with ^{131}I orthoiodohippurate renal scans and reported that there was a 25% mean functional improvement of the targeted kidney at 6 months.[118]

In a number of articles addressing renal functional outcomes, the type of nephrolithotomy procedure used was not described. Stage and Lewis reported on the impact of ANL (technique not described) on GFR, individual percentage contribution to total renal function (PCTRF), and effective RPF as assessed by 131-hippuran and DTPA scintigraphy in six patients. PCTRF improved in three patients with a range of improvement from 5% to 35%, mean GFR improved from 23.2 to 57.6 cc/min, and one patient had a decrease in effective renal plasma flow from 239 to 128 cc/min; overall renal function improved in two patients, decreased in two patients, and remained unchanged in two patients.[119] Similarly, Chen and colleagues followed 24 patients who underwent ANL (technique not described) with ^{131}I hippuran renal scans and noticed close to a 30% decrease in mean effective renal plasma flow (ERPF) in the operated kidney.[120] Kawamura and associates demonstrated an 11.7% mean decrease in renal cortical uptake of DMSA in the kidneys of 22 patients at 1 to 3 months after nephrolithotomy (technique not described). In addition, DMSA scans were performed at 24 months postoperatively in six patients; one patient had increased renal uptake, one was unchanged from preoperative values, and the remainder had decreased renal uptake.[121]

The combination of pyelolithotomy and nephrolithotomy(ies) has been used to remove large renal stones. Balbay and associates studied 12 patients who underwent nephrolithotomy without pyelolithotomy with DMSA scans and there was a 16% mean decrease in tracer uptake in the operated renal unit at 1 month and 10.8% at 3 months; the latter is not statistically significant.[122] This approach has also been used in patients with compromised renal function or solitary kidneys. Witherow and Wickham reported on 19 patients with renal insufficiency and creatinine clearance $\leq$ 20 mL/min subjected to such a procedure. The mean creatinine clearance increased significantly from 12.9 to 25.4 mL/min (mean follow-up of 6.3 years), preventing the need for dialysis.[123] They also described their experience with 29 patients with solitary kidneys.[124] Serum creatinine levels rose in all patients immediately after the operation; however, at a mean follow-up of 26 months, 19 of the 29 patients had return of their creatinine to baseline, 8 experienced a reduction in creatinine, and 2 had a significant increase. Singh and colleagues prospectively evaluated 70 patients with renal stones and varying degrees of CRI of which 63 underwent this combination procedure. They measured GFR from DTPA scans 6 to 9 months postoperatively and reported mean increases in this parameter. This included a 27% increase in those with mild CRI (serum creatinine $<$ 2.0 mg/dL), 14% in those with moderate CRI (serum creatinine 2.0 to 4.0 mg/dL), and 11% in those with severe CRI (serum creatinine $>$ 4.0 mg/dL).[125] Androulakakis and associates evaluated 19 children with staghorn calculi who were treated similarly and demonstrated no functional loss as measured by DMSA renal scans.[126] Al-Kohlany and associates assessed renal function with MAG3 scans in patients harboring staghorn stones who were treated with open surgery, including modified ANL, extended pyelolithotomy, and combined pyelolithotomy/nephrolithotomy. They found no significant decline in the involved renal unit at a mean of 4.9 months after these procedures; results were not segregated by technique.[87]

Pyelolithotomy was once frequently used and occasionally is still undertaken. There are limited functional data reported on this procedure. Eterović and associates evaluated 30 patients who underwent pyelolithotomy with DTPA and ^{131}I hippuran renal scans preoperatively and 3 months postoperatively. Effective RPF increased 72% in the treated kidney at 3 months. GFR increased 81% at 3 months postoperatively.[40]

Few investigators have reviewed the impact of repetitive stone-removing procedures on renal function. Assimos and associates determined the potential impact of cystinuria and cystine stone formation on renal function compared with calcium oxalate stone formers. Evaluation of 40 cystinuric patients demonstrated that an increasing number of open surgical stone-removing procedures was associated with increased serum creatinine; interestingly, number of SWL procedures and a number of percutaneous nephrostolithotomy procedures were not statistically significant.[127] These results suggest that open stone-removing procedures, more so than other treatment modalities, may have

Table 5
The Effects of Open Procedure for Stone Removal on Kidney Function

Study	Measurement	Follow-Up (mo)	Results
Wadhwa P et al (2007)[52]	DMSA, DTPA, EDC	3	No change in GFR or split renal function No new cortical scars
Mahmud M, Zaidi Z (2004)[105]	DMSA	1.5	No new cortical scars
Desai MR et al (2004)[106]	DMSA, Serum creatinine	3-6, 12	No new cortical scars No change in creatinine
Mor Y et al (1997)[108]	DMSA, DTPA, MAG3	23	No decline in function
Dawaba MS et al (2004)[109]	DMSA, DTPA	40	Significant increase in GFR No new cortical scars
Samad L et al (2007)[107]	DMSA	3.6	New cortical defects in 5% of patients

EDC, ^{99m}Tc-ethylene dicystine; DMSA, dimercaptosuccinic acid; DTPA, ^{99m}Tc-diethylenetriaminepentaacetic acid; GFR, glomerular filtration rate; MAG3, ^{99m}Tc-mercaptoacetyltriglycine.

a negative impact on renal function. This deterioration may be more pronounced in the setting of multiple procedures.

Laparoscopic ANL for a staghorn calculus was first described in 2003 in a porcine model[128] and performed in a human a year later by Deger and associates.[129] A nonclassical technique has been used in these cases with no identification of an anatrophic plane and/or utilization of ischemic hypothermia. Kaouk and associates injected polyurethane in the collecting systems of 10 swine to create a staghorn stone surrogate and 2 weeks later removed them via laparoscopic nephrolithotomy in which the whole renal hilum was occluded. GFR was assessed before and 4 to 5 weeks later with DTPA renal scans. The mean total GFR increased from 26.4 mL/min to 54.8 mL/min.[128] Simforoosh and colleagues reviewed a case series of five patients harboring staghorn stones who underwent laparoscopic modified ANL (no demarcation, no ischemic hypothermia) in which only the renal artery was occluded. There was a mean rise in serum creatinine from 1.1 mg/dL preoperatively to 1.8 mg/dL at 6 hours postoperatively.[130] No long-term follow-up data are available. The feasibility of robotic pyelolithotomy has been demonstrated, but renal functional outcomes from these procedures have not been studied (Table 5, Table 6).[131]

Ureteroscopy

There is limited information on the impact of retrograde ureteroscopic stone removal, a commonly performed procedure, on renal function. The renal parenchyma is not typically violated with this procedure. Therefore, a negative impact on renal function is not expected unless egress of urine flow is attenuated by the development of a stricture in the ureter or renal collecting system. Thomas and colleagues demonstrated that pediatric ureteroscopy had no detrimental effects on renal function or growth as measured by quantitative renal scans and excretory urography.[132] Lee and Bagley reported on 18 patients with mild to moderate renal insufficiencies (baseline serum creatinine > 1.5 mg/dL) who were subjected to ureteroscopic stone removal. At mean follow-up of 18 months, GFR (the reciprocal of serum creatinine was used) was 5.9% higher.[133]

Conclusions

There is no question that stone removal can improve renal function by eradicating obstruction and, in certain cases, underlying infection. However, the stone-removing procedure may itself negatively impact the functional integrity of the targeted kidney and perhaps its mate. The presence of renal injury depends on the magnifying glass used for assessment. If parameters such as serum creatinine, estimated GFR, renal plasma flow, and GFR are used, the impact typically is transient and usually negligible; however, if markers of cellular injury and histologic analyses are used, renal injury may be more evident. In addition, the time period used for assessment may be influential as acute renal functional deterioration typically resolves and more chronic

Table 6
Open Procedure Technique for Stone Removal and Kidney Function

Study	Parameter	Follow-Up (mo)	Effects on Renal Fx	Population Specifics
		Classical		
Kijvikai K et al (2004)[115]	DTPA	1.5	9% reduction	
Gough DC, Baillie CT (2000)[114]	DMSA	4	6%-16% reduction	Children
Demler JW et al (1983)[113]	Serum creatinine		No change	Bilateral procedure
Thomas R et al (1981)[111]	131-iodine hippuran	13.6	30% reduction	
Stubbs AJ et al (1978)[112]	Serum creatinine	72	No change	Solitary kidneys
		Modified		
Ramakrishnan PA et al (2006)[116]	DMSA	6	55% stable, 32% improved, 13% worsened (% of cohort)	
Kijvikai K et al (2004)[115]	DTPA	1.5	27% reduction	
Morey AF et al (1999)[117]	DMSA		4% reduction	
Belis JA et al (1981)[118]	131-iodine hippuran	6	25% improvement	
		Undefined		
Chen KK et al (1992)[120]	131-iodine hippuran		30% reduction	
Kawamura J et al (1983)[121]	DMSA	1-3	12% reduction	

DMSA, dimercaptosuccinic acid; DTPA, ^{99m}Tc-diethylenetriaminepentaacetic acid; FX, function.

injury may be more difficult to quantify. Our review suggests that, in most instances, renal functional integrity is preserved after stone removal, and when renal dysfunction does occur, it is typically clinically insignificant.

We have uncovered gaps in knowledge and limitations in the research that has been undertaken on this subject. Much of the information has been generated from animal models; the majority of these studies are short term. As previously mentioned, the tools used for measuring longitudinal renal function have been crude. The cumulative impact of multiple procedures has not been measured in animal or clinical studies. Information regarding the effects on certain populations who are at risk for developing renal insufficiency and also frequently requiring repetitive stone-removing procedures such as those with cystinuria, primary hyperoxaluria, and renal tubular acidosis is limited or lacking. More information regarding the impact of retrograde ureteroscopic stone removal is needed as, theoretically, this approach may be functionally optimal because the parenchyma is not violated. ■

References

1. Chaussy C, Brendel W, Schmiedt E. Extracorporeally induced destruction of kidney stones by shock waves. *Lancet*. 1980;316:1265-1268.
2. McAteer JA, Evan AP. The acute and long-term adverse effects of shock wave lithotripsy. *Semin Nephrol*. 2008;28:200-213.
3. Crum LA. Cavitation microjets as a contributory mechanism for renal calculi disintegration in ESWL. *J Urol*. 1988;140:1587-1590.
4. Zhong P, Tong HL, Cocks FH, Preminger GM. Transient oscillation of cavitation bubbles near stone surface during electrohydraulic lithotripsy. *J Endourol*. 1997;11:55-61.
5. Coleman AJ, Saunders JE, Crum LA, Dyson M. Acoustic cavitation generated by an extracorporeal shockwave lithotripter. *Ultrasound Med Biol*. 1987;13:69-76.
6. Bailey MR, Pishchalnikov YA, Sapozhnikov OA, et al. Cavitation detection during shock-wave lithotripsy. *Ultrasound Med Biol*. 2005;31: 1245-1256.
7. Chen H, Brayman AA, Bailey MR, Matula TJ. Blood vessel rupture by cavitation. *Urol Res*. 2010;38:321-326.
8. Evan AP, Willis LR, McAteer JA, et al. Kidney damage and renal functional changes are minimized by waveform control that suppresses cavitation in shock wave lithotripsy. *J Urol*. 2002; 168:1556-1562.
9. Gunasekaran S, Donovan JM, Chvapil M, Drach GW. Effects of extracorporeal shock wave lithotripsy on the structure and function of rabbit kidney. *J Urol*. 1989;141:1250-1254.
10. Preminger GM. Review: in vivo effects of extracorporeal shock wave lithotripsy: animal studies. *J Endourol*. 1993;7:375-378.
11. Evan AP, Willis LR, Connors B, et al. Shock wave lithotripsy-induced renal injury. *Am J Kidney Dis*. 1991;17:445-450.
12. Karlsen SJ, Berg KJ. Acute changes in renal function following extracorporeal shock wave lithotripsy in patients with a solitary functioning kidney. *J Urol*. 1991;145:253-256.
13. Delvecchio F, Auge BK, Munver R, et al. Shock wave lithotripsy causes ipsilateral renal injury remote from the focal point: the role of regional vasoconstriction. *J Urol*. 2003;169:1526-1529.
14. Newman R, Hackett R, Senior D, et al. Pathologic effects of ESWL on canine renal tissue. *Urology*. 1987;29:194-200.
15. Willis LR, Evan AP, Connors BA, et al. Shock-wave lithotripsy: dose-related effects on renal structure, hemodynamics, and tubular function. *J Endourol*. 2005;19:90-101.

16. Connors BA, Evan AP, Willis LR, et al. The effect of discharge voltage on renal injury and impairment caused by lithotripsy in the pig. *J Am Soc Nephrol*. 2000;11:310-318.
17. Delius M, Jordan M, Eizenhoefer H, et al. Biological effects of shock waves: kidney haemorrhage by shock waves in dogs—administration rate dependence. *Ultrasound Med Biol*. 1988;14:689-694.
18. Evan AP, Connors BA, Pennington DJ, et al. Renal disease potentiates the injury caused by SWL. *J Endourol*. 1999;13:619-628.
19. Evan AP, Willis LR, Lingeman JE, et al. Renal trauma and the risk of long-term complications in shock wave lithotripsy. *Nephron*. 1998;78:1-8.
20. Willis LR, Evan AP, Connors BA, et al. Effects of extracorporeal shock wave lithotripsy to one kidney on bilateral glomerular filtration rate and PAH clearance in minipigs. *J Urol*. 1996;156:1502-1506.
21. Connors BA, Evan AP, Willis LR, et al. Renal nerves mediate changes in contralateral renal blood flow after extracorporeal shockwave lithotripsy. *Nephron Physiol*. 2003;95:67-75.
22. Neal DE Jr, Kaack MB, Harmon EP, et al. Renin production after experimental extracorporeal shock wave lithotripsy: a primate model. *J Urol*. 1991;146(2 Pt 2):548-550.
23. Handa RK, Evan AP, Willis LR, et al. Renal functional effects of multiple-tract percutaneous access. *J Endourol*. 2009;23:1951-1956.
24. Kaji DM, Xie HW, Hardy BE, et al. The effects of extracorporeal shock wave lithotripsy on renal growth, function and arterial blood pressure in an animal model. *J Urol*. 1991;146(2 Pt 2):544-547.
25. Claro Jde A, Denardi F, Ferreira U, et al. Effects of extracorporeal shockwave lithotripsy on renal growth and function: an animal model. *J Endourol*. 1994;8:191-194.
26. Kaude JV, Williams CM, Millner MR, et al. Renal morphology and function immediately after extracorporeal shock-wave lithotripsy. *AJR Am J Roentgenol*. 1985;145:305-313.
27. Baumgartner BR, Dickey KW, Ambrose SS, et al. Kidney changes after extracorporeal shock wave lithotripsy: appearance on MR imaging. *Radiology*. 1987;163:531-534.
28. Rubin JI, Arger PH, Pollack HM, et al. Kidney changes after extracorporeal shock wave lithotripsy: CT evaluation. *Radiology*. 1987;162:21-24.
29. Dhar NB, Thornton J, Karafa MT, Streem SM. A multivariate analysis of risk factors associated with subcapsular hematoma formation following electromagnetic shock wave lithotripsy. *J Urol*. 2004;172:2271-2274.
30. Krishnamurthi V, Streem SB. Long-term radiographic and functional outcome of extracorporeal shock wave lithotripsy induced perirenal hematomas. *J Urol*. 1995;154:1673-1675.
31. Liguori G, Trombetta C, Bucci S, et al. Reversible acute renal failure after unilateral extracorporeal shock-wave lithotripsy. *Urol Res*. 2004;32:25-27.
32. Baskin LS, Stoller ML. Severe haemorrhage after extracorporeal shock wave lithotripsy: radiological evaluation. *Br J Urol*. 1992;69:214-215.
33. Dumont M, Marchand L, Laroche B, et al. Scintigraphic evaluation of renal function after extracorporeal shock-wave lithotripsy. *Can Assoc Radiol J*. 1990;41:138-140.
34. Assimos DG, Boyce WH, Furr EG, et al. Selective elevation of urinary enzyme levels after extracorporeal shock wave lithotripsy. *J Urol*. 1989;142:687-690.
35. Recker F, Hofmann W, Bex A, Tscholl R. Quantitative determination of urinary marker proteins: a model to detect intrarenal bioeffects after extracorporeal lithotripsy. *J Urol*. 1992;148:1000-1006.
36. Rutz-Danielczak A, Pupek-Musialik D, Raszeja-Wanic B. Effects of extracorporeal shock wave lithotripsy on renal function in patients with kidney stone disease. *Nephron*. 1998;79:162-166.
37. Lambert EH, Walsh R, Moreno MW, Gupta M. Effect of escalating versus fixed voltage treatment on stone comminution and renal injury during extracorporeal shock wave lithotripsy: a prospective randomized trial. *J Urol*. 2010;183:580-584.
38. Weichert-Jacobsen K, Stöckle M, Loch T, Brüske T. Urinary leakage of tubular enzymes after shock wave lithotripsy. *Eur Urol*. 1998;33:104-110.
39. Jung K, Kirschner P, Wille A, Brien G. Excretion of urinary enzymes after extracorporeal shock wave lithotripsy: a critical reevaluation. *J Urol*. 1993;149:1409-1413.
40. Eterović D, Juretić-Kuscić L, Capkun V, Dujić Z. Pyelolithotomy improves while extracorporeal lithotripsy impairs kidney function. *J Urol*. 1999;161:39-44.

Main Points

- Animal models have demonstrated both histologic and functional changes after shock wave lithotripsy (SWL). Using canine and rabbit models, acute histologic damage to the renal parenchyma, renal vasculature, and the nephron structure was noted. Renal morphologic changes after shock waves include the development of subcapsular hematomas and focal parenchymal damage.
- The literature on SWL tissue effects in human kidneys is limited. SWL has been reported to cause renal and perirenal hematomas in humans, and although symptomatic renal and perirenal hematomas are quite rare, 0.6% to 1.3%, magnetic resonance imaging and computed tomography have demonstrated that subclinical hematomas occur in as many as 25% of patients.
- Various studies suggest that patients with solitary kidneys or those with mild or moderate renal insufficiency will not experience renal functional deterioration after SWL and may even experience benefits due to relief of obstruction. Those with more profound renal insufficiency will typically progress to dialysis dependency that may be a result of the natural history of their renal disease.
- Because the kidneys of children are still developing, there has been concern that SWL may impair renal growth and impact kidney function, although various investigators have reported on the safety of SWL in this young cohort.
- Stone removal can improve renal function by eradicating obstruction and underlying infection; however, the stone-removing procedure may negatively impact the functional integrity of the targeted kidney. If parameters such as serum creatinine, estimated glomerular filtration rate (GFR), renal plasma flow, and GFR are used, the impact typically is transient and usually negligible; if markers of cellular injury and histologic analyses are used, renal injury may be more evident.
- Study results suggest that open stone-removing procedures, more so than other treatment modality, may have a negative impact on renal function. This deterioration may be more pronounced in the setting of multiple procedures.
- There are gaps in knowledge as well as limitations in the research. Much information has been generated from animal models; the majority of these studies are short term. More information regarding the impact of retrograde ureteroscopic stone removal is needed as this approach may be functionally optimal because the parenchyma is not violated. Further research is needed on this subject.

41. Pienkny AJ, Streem SB. Simultaneous versus staged bilateral extracorporeal shock wave lithotripsy: long-term effect on renal function. *J Urol.* 1999;162:1591-1593.
42. Perry KT, Smith ND, Weiser AC, et al. The efficacy and safety of synchronous bilateral extracorporeal shock wave lithotripsy. *J Urol.* 2000;164:644-647.
43. Karlsen SJ, Smevik B, Hovig T. Acute morphological changes in canine kidneys after exposure to extracorporeal shock waves. A light and electron microscopic study. *Urol Res.* 1991;19: 105-115.
44. Kulb TB, Lingeman JE, Coury TA, et al. Extracorporeal shock wave lithotripsy in patients with a solitary kidney. *J Urol.* 1986;136:786-788.
45. Zanetti GR, Montanari E, Guarneri A, et al. Long-term followup after extracorporeal shock wave lithotripsy treatment of kidney stones in solitary kidneys. *J Urol.* 1992;148:1011-1014.
46. Cass AS. Renal function after extracorporeal shock wave lithotripsy to a solitary kidney. *J Endourol.* 1994;8:15-19.
47. Chandhoke PS, Albala DM, Clayman RV. Long-term comparison of renal function in patients with solitary kidneys and/or moderate renal insufficiency undergoing extracorporeal shock wave lithotripsy or percutaneous nephrolithotomy. *J Urol.* 1992;147:1226-1230.
48. Paryani JP, Ather MH. Improvement in serum creatinine following definite treatment of urolithiasis in patients with concurrent renal insufficiency. *Scand J Urol Nephrol.* 2002;36: 134-136.
49. Lottmann HB, Archambaud F, Hellal B, et al. 99mTechnetium-dimercapto-succinic acid renal scan in the evaluation of potential long-term renal parenchymal damage associated with extracorporeal shock wave lithotripsy in children. *J Urol.* 1998;159:521-524.
50. Picramenos D, Deliveliotis C, Alexopoulou K, et al. Extracorporeal shock wave lithotripsy for renal stones in children. *Urol Int.* 1996;56:86-89.
51. Lottmann HB, Archambaud F, Traxer O, et al. The efficacy and parenchymal consequences of extracorporeal shock wave lithotripsy in infants. *BJU Int.* 2000;85:311-315.
52. Wadhwa P, Aron M, Bal CS, et al. Critical prospective appraisal of renal morphology and function in children undergoing shockwave lithotripsy and percutaneous nephrolithotomy. *J Endourol.* 2007;21:961-966.
53. Fayad A, El-Sheikh MG, Abdelmohsen M, Abdelraouf H. Evaluation of renal function in children undergoing extracorporeal shock wave lithotripsy. *J Urol.* 2010;184:1111-1114.
54. Goel MC, Baserge NS, Babu RV, et al. Pediatric kidney: functional outcome after extracorporeal shock wave lithotripsy. *J Urol.* 1996;155: 2044-2046.
55. Marberger M, Türk C, Steinkogler I. Piezoelectric extracorporeal shock wave lithotripsy in children. *J Urol.* 1989;142:349-352.
56. Thornhill JA, Moran K, Mooney EE, et al. Extracorporeal shockwave lithotripsy monotherapy for paediatric urinary tract calculi. *Br J Urol.* 1990;65:638-640.
57. Mishriki SF, Wills MI, Mukherjee A, et al. Extracorporeal shock wave lithotripsy for renal calculi in children. *Br J Urol.* 1992;69:303-305.
58. Thomas R, Frentz JM, Harmon E, Frentz GD. Effect of extracorporeal shock wave lithotripsy on renal function and body height in pediatric patients. *J Urol.* 1992;148:1064-1066.
59. Van Horn AC, Hollander JB, Kass EJ. First and second generation lithotripsy in children: results, comparison and followup. *J Urol.* 1995;153: 1969-1971.
60. Lottmann HB, Traxer O, Archambaud F, Mercier-Pageyral B. Monotherapy extracorporeal shock wave lithotripsy for the treatment of staghorn calculi in children. *J Urol.* 2001;165: 2324-2327.
61. Griffin SJ, Margaryan M, Archambaud F, et al. Safety of shock wave lithotripsy for treatment of pediatric urolithiasis: 20-year experience. *J Urol.* 2010;183:2332-2336.
62. Villányi KK, Székely JG, Farkas LM, et al. Short-term changes in renal function after extracorporeal shock wave lithotripsy in children. *J Urol.* 2001;166:222-224.
63. Reis LO, Zani EL, Ikari O, et al. Extracorporeal lithotripsy in children—the efficacy and long-term evaluation of renal parenchyma damage by DMSA-^{99m}Tc scintigraphy. [Article in Spanish] *Actas Urol Esp.* 2010;34:78-81.
64. Lifshitz DA, Lingeman JE, Zafar FS, et al. Alterations in predicted growth rates of pediatric kidneys treated with extracorporeal shockwave lithotripsy. *J Endourol.* 1998;12:469-475.
65. Fernström I, Johansson B. Percutaneous pyelolithotomy. A new extraction technique. *Scand J Urol Nephrol.* 1976;10:257-259.
66. Michel MS, Trojan L, Rassweiler JJ. Complications in percutaneous nephrolithotomy. *Eur Urol.* 2007;51:899-906; discussion 906.
67. Probst CE, Denstedt JD, Razvi H. Preoperative indications for percutaneous nephrolithotripsy in 2009. *J Endourol.* 2009;23:1557-1561.
68. Webb DR, Fitzpatrick JM. Percutaneous nephrolithotripsy: a functional and morphological study. *J Urol.* 1985;134:587-591.
69. David R, Fuchs G, Barbaric Z. Comparison of bioeffects of open surgery, percutaenous surgery, and extracorporeal shock wave lithotripsy on renal function and morphology in the farm pig: creation of an animal model. *J Endourol.* 1990;4:27-35.
70. Wilson WT, Husmann DA, Morris JS, et al. A comparison of the bioeffects of four different modes of stone therapy on renal function and morphology. *J Urol.* 1993;150:1267-1270.
71. Clayman RV, Elbers J, Miller RP, et al. Percutaneous nephrostomy: assessment of renal damage associated with semi-rigid (24F) and balloon (36F) dilation. *J Urol.* 1987;138:203-206.
72. Al-Kandari AM, Jabbour M, Anderson A, et al. Comparative study of degree of renal trauma between Amplatz sequential fascial dilation and balloon dilation during percutaneous renal surgery in an animal model. *Urology.* 2007;69: 586-589.
73. Traxer O, Smith TG 3rd, Pearle MS, et al. Renal parenchymal injury after standard and mini percutaneous nephrostolithotomy. *J Urol.* 2001; 165:1693-1695.
74. Travis DG, Tan HL, Webb DR. Single-increment dilatation for percutaneous renal surgery: an experimental study. *Br J Urol.* 1991;68:144-147.
75. Handa RK, Matlaga BR, Connors BA, et al. Acute effects of percutaneous tract dilation on renal function and structure. *J Endourol.* 2006;20:1030-1040.
76. Handa RK, Willis LR, Connors BA, et al. Time-course for recovery of renal function after unilateral (single-tract) percutaneous access in the pig. *J Endourol.* 2010;24:283-288.
77. Handa RK, Johnson CD, Connors BA, et al. Renal functional effects of simultaneous bilateral single-tract percutaneous access in pigs. *BJU Int.* 2010;105:125-128.
78. Saxby MF. Effects of percutaneous nephrolithotomy and extracorporeal shock wave lithotripsy on renal function and prostaglandin excretion. *Scand J Urol Nephrol.* 1997;31:141-144.
79. Urivetsky M, Motola J, King L, Smith AD. Impact of percutaneous renal stone removal on renal function: assessment by urinary lysozyme activity. *Urology.* 1989;33:305-308.
80. Trinchieri A, Mandressi A, Zanetti G, et al. Renal tubular damage after renal stone treatment. *Urol Res.* 1988;16:101-104.
81. Alken P. Percutaneous ultrasonic destruction of renal calculi. *Urol Clin North Am.* 1982;9:145-151.
82. Marberger M, Stackl W, Hruby W, Kroiss A. Late sequelae of ultrasonic lithotripsy of renal calculi. *J Urol.* 1985;133:170-173.
83. Ekelund L, Lindstedt E, Lundquist SB, et al. Studies on renal damage from percutaneous nephrolitholapaxy. *J Urol.* 1986;135:682-685.
84. Schiff RG, Lee WJ, Eshghi M, et al. Morphologic and functional changes in the kidney after percutaneous nephrosto-lithotomy. *AJR Am J Roentgenol.* 1986;147:283-286.
85. Eshghi M, Schiff RG, Smith AD. Renal effects of percutaneous stone removal. *Urology.* 1989;33: 120-124.
86. Mayo ME, Krieger JN, Rudd TG. Effect of percutaneous nephrostolithotomy on renal function. *J Urol.* 1985;133:167-169.
87. Al-Kohlany KM, Shokeir AA, Mosbah A, et al. Treatment of complete staghorn stones: a prospective randomized comparison of open surgery versus percutaneous nephrolithotomy. *J Urol.* 2005;173:469-473.
88. Chatham JR, Dykes TE, Kennon WG, Schwartz BF. Effect of percutaneous nephrolithotomy on differential renal function as measured by mercaptoacetyl triglycine nuclear renography. *Urology.* 2002;59:522-525; discussion 525-526.
89. Moskovitz B, Halachmi S, Sopov V, et al. Effect of percutaneous nephrolithotripsy on renal function: assessment with quantitative SPECT of (99m)Tc-DMSA renal scintigraphy. *J Endourol.* 2006;20:102-106.
90. Ünsal A, Koca G, Reşorlu B, et al. Effect of percutaneous nephrolithotomy and tract dilatation methods on renal function: assessment by quantitative single-photon emission computed tomography of technetium-99m-dimercaptosuccinic acid uptake by the kidneys. *J Endourol.* 2010;24:1497-1502.

91. Kiliç S, Altinok T, Altunoluk B, et al. Long-term effects of percutaneous nephrolithotomy on renal morphology and arterial vascular resistance as evaluated by color Doppler ultrasonography: preliminary report. *Urol Res*. 2006;34:178-183.
92. Kiliç S, Oğuz F, Kahraman B, et al. Prospective evaluation of the alterations in the morphology and vascular resistance of the renal parenchyma with color Doppler ultrasonography after percutaneous nephrolithotomy. *J Endourol*. 2008;22:615-621.
93. Handa RK, Evan AP, Willis LR, et al. Renal functional effects of multiple-tract percutaneous access. *J Endourol*. 2009;23:1951-1956.
94. Hegarty NJ, Desai MM. Percutaneous nephrolithotomy requiring multiple tracts: comparison of morbidity with single-tract procedures. *J Endourol*. 2006;20:753-760.
95. Segura JW, Patterson DE, LeRoy AJ, et al. Percutaneous removal of kidney stones: review of 1,000 cases. *J Urol*. 1985;134:1077-1081.
96. Jones DJ, Kellett MJ, Wickham JE. Percutaneous nephrolithotomy and the solitary kidney. *J Urol*. 1991;145:477-479; discussion 479-480.
97. Streem SB, Zelch MG, Risius B, Geisinger MA. Percutaneous extraction of renal calculi in patients with solitary kidneys. *Urology*. 1986;27:247-252.
98. Liou LS, Streem SB. Long-term renal functional effects of shock wave lithotripsy, percutaneous nephrolithotomy and combination therapy: a comparative study of patients with solitary kidney. *J Urol*. 2001;166:36; discussion 36-37.
99. Canes D, Hegarty NJ, Kamoi K, et al. Functional outcomes following percutaneous surgery in the solitary kidney. *J Urol*. 2009;181:154-160.
100. Agrawal MS, Aron M, Asopa HS. Endourological renal salvage in patients with calculus nephropathy and advanced uraemia. *BJU Int*. 1999;84:252-256.
101. Kuzgunbay B, Gul U, Turunc T, et al. Long-term renal function and stone recurrence after percutaneous nephrolithotomy in patients with renal insufficiency. *J Endourol*. 2010;24:305-308.
102. Yaycioglu O, Egilmez T, Gul U, et al. Percutaneous nephrolithotomy in patients with normal versus impaired renal function. *Urol Res*. 2007;35:101-105.
103. Bilen CY, Inci K, Kocak B, et al. Impact of percutaneous nephrolithotomy on estimated glomerular filtration rate in patients with chronic kidney disease. *J Endourol*. 2008;22:895-900.
104. Kukreja R, Desai M, Patel SH, Desai MR. Nephrolithiasis associated with renal insufficiency: factors predicting outcome. *J Endourol*. 2003;17:875-879.
105. Mahmud M, Zaidi Z. Percutaneous nephrolithotomy in children before school age: experience of a Pakistani centre. *BJU Int*. 2004;94:1352-1354.
106. Desai MR, Kukreja RA, Patel SH, Bapat SD. Percutaneous nephrolithotomy for complex pediatric renal calculus disease. *J Endourol*. 2004;18:23-27.
107. Samad L, Qureshi S, Zaidi Z. Does percutaneous nephrolithotomy in children cause significant renal scarring? *J Pediatr Urol*. 2007;3:36-39.
108. Mor Y, Elmasry YE, Kellett MJ, Duffy PG. The role of percutaneous nephrolithotomy in the management of pediatric renal calculi. *J Urol*. 1997;158:1319-1321.
109. Dawaba MS, Shokeir AA, Hafez AT, et al. Percutaneous nephrolithotomy in children: early and late anatomical and functional results. *J Urol*. 2004;172:1078-1081.
110. Matlaga BR, Assimos DG. Changing indications of open stone surgery. *Urology*. 2002;59:490-493; discussion 493-494.
111. Thomas R, Lewis RW, Roberts JA. The renal quantitative scintillation camera study for determination of renal-function after anatrophic nephrolithotomy. *J Urol*. 1981;125:287-288.
112. Stubbs AJ, Resnick MI, Boyce WH. Anatrophic nephrolithotomy in the solitary kidney. *J Urol*. 1978;119:457-460.
113. Demler JW, Dennis MA, Finlayson B. Bilateral nephrolithiasis: simultaneous operative management. *J Urol*. 1983;129:263-265.
114. Gough DC, Baillie CT. Paediatric anatrophic nephrolithotomy; stone clearance—at what price? *BJU Int*. 2000;85:874-878.
115. Kijvikai K, Leenanupunth C, Sirisrio R, Lertsithichai P. Comparative study of renal function between standard and modified anatrophic nephrolithotomy by radionuclide renal scans. *J Med Assoc Thai*. 2004;87:704-708.
116. Ramakrishnan PA, Al-Bulushi YH, Medhat M, et al. Modified anatrophic nephrolithotomy: A useful treatment option for complete complex staghorn calculi. *Can J Urol*. 2006;13:3261-3270.
117. Morey AF, Nitahara KS, McAninich JW. Modified anatrophic nephrolithotomy for management of staghorn calculi: is renal function preserved? *J Urol*. 1999;162:670-673.
118. Belis JA, Morabito RA, Kandzari SJ, et al. Anatrophic nephrolithotomy: preservation of renal function demonstrated by differential quantitative radionuclide renal scans. *J Urol*. 1981;125:761-764.
119. Stage KH, Lewis S. Pre- and postoperative evaluation of renal function in patients with staghorn calculi utilizing quantitative renal scanning. *Urology*. 1981;17:29-32.
120. Chen KK, Chen MT, Yeh SH, Chang LS. Radionuclide renal function study in various surgical treatments of upper urinary stones. *Zhonghua Yi Xue Za Zhi (Taipei)*. 1992;49:319-327.
121. Kawamura J, Itoh H, Okada Y, et al. Preoperative and postoperative cortical function of the kidney with staghorn calculi assessed by 99mtechnetium-dimercaptosuccinic acid renal scintigraphy. *J Urol*. 1983;130:430-433.
122. Balbay MD, Varoğlu E, Devrim H, et al. Quantitative evaluation of renal parenchymal mass with 99mtechnetium dimercapto-succinic acid scintigraphy after nephrolithotomy. *J Urol*. 1997;157:1226-1228.
123. Witherow RO, Wickham JE. Nephrolithotomy in chronic renal failure: saved from dialysis! *Br J Urol*. 1980;52:419-421.
124. Perry NM, Wickham JE, Whitfield HN. Hypothermic nephrolithotomy in solitary kidneys. *Br J Urol*. 1980;52:415-418.
125. Singh I, Gupta NP, Hemal AK, et al. Efficacy and outcome of surgical intervention in patients with nephrolithiasis and chronic renal failure. *Int Urol Nephrol*. 2001;33:293-298.
126. Androulakakis PA, Michael V, Polychronopoulou S, Aghioutantis C. Evaluation of open surgery for staghorn calculi in children. *Child Nephrol Urol*. 1990;10:139-142.
127. Assimos DG, Leslie SW, Ng C, et al. The impact of cystinuria on renal function. *J Urol*. 2002;168:27-30.
128. Kaouk JH, Gill IS, Desai MM, et al. Laparoscopic anatrophic nephrolithotomy: feasibility study in a chronic porcine model. *J Urol*. 2003;169:691-696.
129. Deger S, Tuellmann M, Schoenberger B, et al. Laparoscopic anatrophic nephrolithotomy. *Scand J Urol Nephrol*. 2004;38:263-265.
130. Simforoosh N, Aminsharifi A, Tabibi A, et al. Laparoscopic anatrophic nephrolithotomy for managing large staghorn calculi. *BJU Int*. 2008;101:1293-1296.
131. Badani KK, Hemal AK, Fumo M, et al. Robotic extended pyelolithotomy for treatment of renal calculi: a feasibility study. *World J Urol*. 2006;24:198-201.
132. Thomas R, Ortenberg J, Lee BR, Harmon EP. Safety and efficacy of pediatric ureteroscopy for management of calculous disease. *J Urol*. 1993;149:1082-1084.
133. Lee DI, Bagley DH. Long-term effects of ureteroscopic laser lithotripsy on glomerular filtration rate in the face of mild to moderate renal insufficiency. *J Endourol*. 2001;15:715-717.