Percutaneous Access: Acute Effects on Renal Function and Structure in a Porcine Model


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Abstract. Percutaneous nephrolithotomy (PCNL) involves gaining access into the urinary collecting system to remove kidney stones. Animal studies demonstrated that a reduction in renal filtration and perfusion in both kidneys, and a decline in tubular organic anion transport in the treated kidney characterizes the acute (hours) functional response to unilateral percutaneous access. The acute morphologic and histological changes in the treated kidney were consistent with blunt trauma and ischemia. Only tubular organic anion transport remained depressed during the late (3-day) response to the access procedure. Human studies revealed an acute decline in glomerular function and bilateral renal vasoconstriction following unilateral PCNL. Therefore, percutaneous access is not a benign procedure, but is associated with acute functional and structural derangements.

Keywords: Percutaneous access; percutaneous nephrolithotomy; tract dilation; kidney function.

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INTRODUCTION

Percutaneous nephrolithotomy (PCNL) has replaced open surgery as the preferred method to treat complex kidney stone disease. The procedure involves needle puncture from the skin surface into the urinary collecting system, which is then dilated and stabilized for the introduction of instrumentation that can view and remove stones. PCNL is associated with high stone free rates, low re-treatment rates, low incidence of complications and morbidity, as well as shorter durations in surgery and convalescence compared to open stone surgery [1-6]. Consequently, PCNL is regarded as a safe and efficient method for the treatment of nephrolithiasis.

Postoperative measurements of renal function have generally been taken several weeks, months or years after PCNL, and indicate that renal function is well preserved
[7-10]. However, the immediate effects on renal function are unknown, and it is unclear whether surgical procedures—indeed of stone removal—alter kidney function acutely. Nor is it known whether the two most common methods of dilating the percutaneous access tract—balloon and serial dilators—have similar or differing effects on renal function and structure. We have begun to address these and other issues in a pig model and in patients, and provide the reader with some of our findings.

**ANIMAL STUDIES: ACUTE FUNCTIONAL EFFECTS OF PERCUTANEOUS ACCESS**

Adult farm swine (70 kg) were anesthetized and prepared for renal function measurements using inulin and *para*-aminohippuric acid (PAH) clearance methods as previously described [11]. Experienced urologists gained percutaneous access to a lower pole calyx using procedures identical to that performed on patients [12]. Tract dilation was achieved with either balloon or serial semi-rigid dilator systems, followed by placement of a 30 French working-sheath.

Access with either dilator system had similar effects on renal function (Fig. 1). There was an initial fall in glomerular filtration rate (GFR) and renal plasma flow (RPF) of ~50% that remained depressed during the entire post-surgery observation period (Fig. 1A-B). The renal extraction of PAH from the blood (EPAH) was also significantly reduced following the percutaneous access procedure (Fig. 1C). PAH is largely extracted from the blood into the lumens of renal tubules by specific and selective organic anion transporters located on the membranes of renal tubular epithelial cells [13-15], and provides one measure of proximal tubule transport activity. Hence, the decrease in EPAH suggests that percutaneous access is associated with a reduction in the elimination of organic anions by the kidney.

There were also effects on the contralateral, untreated kidney, i.e., reduced GFR and RPF, but not EPAH (Fig. 1D-F). The mechanism(s) involved in mediating the hemodynamic changes in the untreated kidney are unknown, but similar bilateral renal effects have been observed after unilateral shock wave lithotripsy and largely involved renal sympathetic nerves [16].

Therefore, unilateral percutaneous access results in bilateral renal vasoconstriction and unilateral reduction in tubular organic anion transport.

**ANIMAL STUDIES: ACUTE STRUCTURAL EFFECTS OF PERCUTANEOUS ACCESS**

At the completion of functional measurements (see “Animal Studies: Acute Functional Effects of Percutaneous Access”), kidneys were perfusion fixed *in vivo* and removed for routine histopathology or whole-kidney serial sectioning for morphological analysis [17].

Balloon and semi-rigid dilator systems resulted in similar effects on renal morphology and histology. The access procedure created an open channel (asterisk)
FIGURE 1. Unilateral percutaneous access (Perc) on bilateral renal function in pigs subjected to sham dilation (n = 8), serial semi-rigid dilators (n = 8) or balloon dilation (n = 7). Data are presented as means ± SEM. * = P<0.05 from pre-Perc value using mixed-effect models.

from the renal surface to the papillary tip. The channel was surrounded by an irregular zone of injured parenchyma (arrows) that was on average 2-fold larger in area than the size of the tract (Fig. 2).

Vascular injury included congestion of peritubular capillaries and intraparenchymal hemorrhage resulting from lacerated arcuate veins and arteries. Cellular injury included apical blebbing, vacuolization and necrosis. There was also protein present in the tubules (tubular casts), which reflects injury to the glomerular filtration barrier. All the morphological and histological changes were indicative of blunt trauma and ischemia [18].
ANIMAL STUDIES: SHORT-TERM RECOVERY PROFILE AFTER PERCUTANEOUS ACCESS

Renal hemodynamic and tubular function was measured following 3 days of recovery from percutaneous access surgery. This time frame was chosen, in part, because the status of renal function is unknown at a time when urologists may regain access through the existing tract to remove any residual stones. Animals were anesthetized and renal function measurements were performed before and 1 hour after percutaneous access with a balloon dilator. Animals were allowed to regain consciousness and were then anesthetized 3 days later for final measurements of renal function, including sampling of renal venous blood for measurement of EPAH and calculation of RPF.

A decrease in GFR and effective RPF (ERPF) occurred in the instrumented kidney immediately following percutaneous access and returned to pre-operative levels within 3 days (Fig. 3A-B); EPAH remained depressed in the treated kidney at the 3-day measurement (Fig. 3C). We presume that the reduced EPAH is reflective of the destruction, injury and trauma to the renal tubules following surgery.

ERPF is determined by measuring renal PAH clearance and provides an approximation of RPF with the assumption that all of the PAH is removed from the blood in one passage through the kidney. To obtain a true value of RPF, the fractional removal of PAH from the arterial blood must be determined, i.e. EPAH, and the renal function returns to normal levels within 3 days.
clearance of PAH appropriately corrected [19]. RPF calculations indicate that renal perfusion in the treated kidney tended to be ~50% higher than in the contralateral untreated kidney, or sham-treated kidneys at the 3-day measurement (Fig. 3D). Although the increase in RPF did not reach a level of statistical significance, it suggests that there is a trend for the treated kidney to be in a state of hyperperfusion 3 days after percutaneous access. A direct measurement of regional renal perfusion rates will establish whether this is indeed the case, and also if the elevated perfusion is global or focal to the site of injury.

**HUMAN STUDIES: ACUTE RENAL EFFECTS OF PCNL**

We performed a retrospective analysis of stone formers who underwent unilateral PCNL with single access at our institution between July 2002 and May 2004. A total of 196 patients with normal pre-operative serum creatinine (Cr) of ≤ 1.5 mg/dL were included in this analysis. Urologists gained access in the operating room using a technique that has been previously described [12]. Tract dilation was accomplished and maintained with a balloon dilating system and a 30 French working-sheath, respectively. Both rigid and flexible nephroscopy with intracorporeal lithotripsy were
employed for stone removal. A 10 French Cope loop nephrostomy tube was routinely placed at the end of the procedure. Serum Cr was measured pre-operatively and 1 day post-PCNL to assess renal glomerular function.

Figure 4 shows the patient-distribution curve of the Cr response to PCNL. Serum Cr increased from 0.97 ± 0.02 mg/dL to 1.11 ± 0.02 mg/dL ($\Delta = 0.14 \pm 0.02$ mg/dL, $P<0.001$) following PCNL in all patients. Breakdown of the responses revealed that some patients experienced a decline (33/196), no change (37/196) or a rise (126/196) in serum Cr. The latter cohort of patients exhibited ~28% higher serum Cr values after PCNL compared to their pre-operative level of 0.95 ± 0.02 mg/dL. Therefore, PCNL produced an acute decline in renal glomerular function in most patients. Although, these results do not inform whether one or both kidneys contributed to the rise in serum Cr, they do support our findings in animals that the PCNL procedure results in an acute decline in renal glomerular function.

![Figure 4](image.png)

**FIGURE 4.** Change in 24-hour serum creatinine levels after unilateral PCNL.

Figure 5 shows nuclear renographs from a 29-year-old female patient who underwent unilateral PCNL with single access to remove kidney stones. Renal imaging of intravenously administered 99mTc-mecaptoacetyl triglycine (MAG3) to estimate ERPF was performed before (Fig. 5A) and immediately after PCNL (Fig. 5B), and 30 days post-surgery (Fig. 5C). Split renal function measurements obtained about 2 hours after PCNL revealed that ERPF fell from pre-operative values by 56% and 22% in the PCNL-treated right kidney (radionuclide-filled nephrostomy tube can be seen on image) and untreated left kidney, respectively. At 30 days post-PCNL, ERPF was at normal values in the untreated kidney and approximately 83% recovered in the PCNL-treated kidney. Therefore, the acute response to unilateral PCNL in this patient was bilateral renal vasoconstriction, similar to what we had previously observed in our animal model.
SUMMARY AND CONCLUSIONS

Unilateral percutaneous access with serial or balloon dilators resulted in similar acute (hours) declines in porcine renal filtration and perfusion, and tubular transport function, i.e. vasoconstriction in both kidneys with decreased tubular organic anion transport localized to the treated kidney. Both tract dilation procedures showed similar structural changes consistent with blunt trauma and ischemia. Short-term (3-day) recovery from percutaneous access surgery demonstrated that renal hemodynamic function had largely recovered, whereas the kidney’s ability to eliminate organic anions, and perhaps organic cations, in the urine remained impaired. This could potentially have important clinical implications as these renal tubular transporters are primarily involved in the elimination of many drugs, toxins and endogenous compounds from the body. Finally, unilateral PCNL in human patients resulted in an acute decline in glomerular function, and initial renal perfusion imaging of a single patient indicated that PCNL was also associated with bilateral renal vasoconstriction. The similarity of human and animal responses to the percutaneous access procedure suggests that the pig may be a good model to study the human renal response to PCNL.

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REFERENCES