A Comparative Study of Retrograde Insertion of a Ureteral Catheter or Not in Total Tubeless Percutaneous Nephrolithotomy

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1. **Title**: A Comparative Study of Retrograde Ureteral Catheter Insertion or Not in Total Tubeless Percutaneous Nephrolithotomy
2. **Registered：** It is intended to be registered in the International Clinical Trial Registry (www.clinicaltrials.gov/).
3. **Trial protocol version and date**: Version3.0/October 8, 2022
4. **Funding Project**: This study was supported by the Clinical Research Project of University of South China (USCKF201902K01), and the Hunan Provincial Clinical Medical Technology Innovation Guiding Project (2020SK51801).
5. **Study participants and responsibilities**: one experienced associate chief urologist performed the surgery, and at least 3-5 researchers participated in data collection and analysis.
6. **The research background and theory**: Total tubeless Percutneous nephrolithotomy (PCNL) is a modified surgical method of PCNL surgery, that is, there is no indwelling nephrostomy tube and double-J tube during PCNL surgery. Compared with traditional PCNL surgery, it has the advantages of reducing pain, shortening operation time, and reducing operation cost. Since this procedure was first performed in 2004, several randomized clinical studies have verified the safety and efficacy of total tubeless PCNL. With the continuous development of minimally invasive surgery, since the successful implementation of tubeless PCNL in 1997, several randomized controlled clinical studies have verified the safety and feasibility of total tubeless PCNL surgery. With the continuous update of ultrasound equipment and the continuous progress of physician puncture technology, the application of ultrasound guided PCNL surgery is more and more popular. Moreover, ultrasound-guided percutaneous renal aspiration is increasingly independent of retrograde pyelography or artificial hydronephrosis. Therefore, PCNL without reverse insertion of a ureteral catheter has been attempted, especially when patients with severe rheumatoid arthritis or hip ankylosis are clinically encountered, and the lithotomy position is not possible. Passive PCNL without

reverse insertion of ureteral catheter has been successfully performed. Therefore, it is theoretically feasible to carry out total tubeless PCNL without reverse insertion of a ureteral catheter for patients with unobstructed urinary drainage.

7. **Study objective**: The purpose of this study was to evaluate whether without retrograde ureteral catheterization is appropriate for total tubeless PCNL.
8. **Experimental design**: Parallel group design, a total of 2 groups (total tubeless PCNL group without reverse insertion of a ureteral catheter and conventional total tubeless PCNL group) were allocated according to 1:1 or approximately 1:1 for exploratory study.
9. **Study site**: Single-center study, conducted in the Department of Urology, The First Affiliated Hospital of the University of South China.
10. **Inclusion and exclusion criteria**: Inclusion criteria: (1) patients with kidney stones who met the indications for PCNL surgery; (2) the maximum diameter is less than 35mm; (3) the width of hydronephrosis effusion was less than 25mm. exclusion criteria :(1) patients with infectious calculi confirmed by preoperative CT examination and blood biochemical indexes; (2) Patients with severe cardiac and pulmonary insufficiency, coagulation dysfunction and other obvious surgical contraindications; (3) Patients with previous history of PCNL surgery on the affected side or nephrotomy; (4) Patients with indwelling double J tube or nephrostomy tube before operation; (5) Patients with renal trauma or congenital anomalies of urinary system.
11. **Intervention measures**: a. Total tubeless PCNL without reverse insertion of a ureteral catheter and conventional total tubeless PCNL were performed according to the group, and the same deputy chief physician of urology performed the operation according to the random group; B. Symptomatic treatment of patients during perioperative period is allowed, including antiinfection, analgesia, etc.

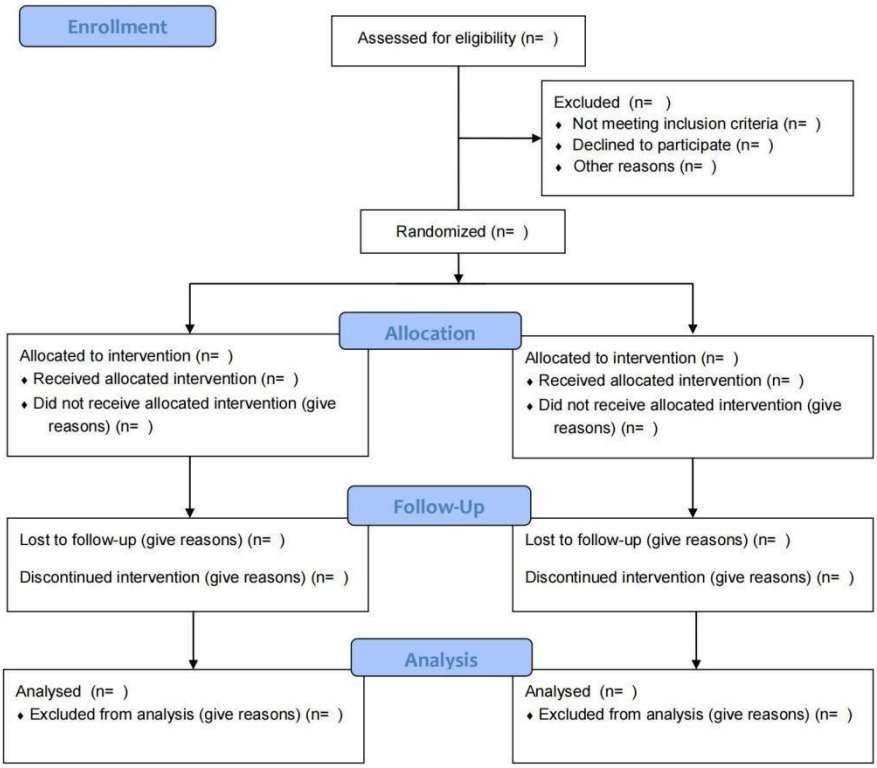
Total tubeless PCNL without reverse insertion of a ureteral catheter implementation process: endotracheal intubation in patients with general anesthesia, prone position after detaining urethral catheter, used in ultrasound guided puncture needle percutaneous renal biopsy to appropriate calyces, under the direct observation of needle in the renal collecting system, using fascia dilator under guide wire step by step coaxial expansion of percutaneous renal channel to 16 Fr or 18 Fr. A rigid nephroscope was inserted and the stone was broken by holmium laser. The crushed stones were removed from the body using constant flow perfusion during stone crushing and stone removal. After checking that there was no residual "visible stone", the puncture sheath was slowly withdrawn, the skin-kidney channel was checked for active bleeding, and the skin incision was closed with suture.

The implementation process of conventional total tubeless PCNL: Endotracheal intubation in patients with general anesthesia, patients were placed in a lithotomy position, and ureteral catheter was inserted reversely under transurethral ureteroscopy and fixed on the urinary catheter. Then, the patients were moved to a prone position and were disinfected again, under the guidance of ultrasound in establishing a channel process and stone removal process was the same as that in total tubeless PCNL without reverse insertion of a ureteral catheter, after inspection without the "visible" stone of residual, The puncture sheath was slowly withdrawn, the passage was checked for active bleeding, and the skin incision was closed with suture.

12. **Outcome indicators**: The primary end point was the rate of postoperative complications, Observation indexes including postoperative fever, inflammation index change (postoperative blood leukocytes and neutrophils ratio changes value), hemorrhage (postoperative hemoglobin change value, red blood cell pressure change value and the incidence of renal subcapsular hematoma), kidney damage (postoperative serum creatinine change value),

pain (postoperative VAS pain score, non-steroidal anti-inflammatory analgesic and opioids Rate) and the incidence of pleural effusion. Secondary end points included stone free rate, operation time, postoperative hospital stay, and hospital costs.

13. **Study flow charts**



14. **Sample size**: a total of 100 subjects are expected to be included (50 in each group).
15. **Recruitment of study subjects**: Recruiting research subjects were conducted by a researcher in the Urology Clinic of the First Affiliated Hospital of the University of South China.
16. **Allocation sequence generation and implementation method**: A researcher was assigned to the group by random number method (odd number represents the conventional tubeless PCNL, and even number represents the total tubeless PCNL without reverse insertion of a ureteral catheter), which took place in the operating room.

17. **Blinding method**: single-blind, the enrolled patients were only told that they could receive either of the two surgical procedures, and the specific surgical method was determined by random number table method after entering the operating room.
18. **Data collection**. All data to be measured: 1. Demographic data, stone characteristics, and preoperative baseline data, Including the proportion of gender, age, body mass index (BMI) and basic diseases distribution, location, stones, stone maximum cross-sectional area, the width of hydronephrosis, preoperative hemoglobin, Preoperative hematocrit, preoperative blood leukocyte count, preoperative blood neutrophils ratio, preoperative serum creatinine, urine leucocyte, site of puncture and operation laterality, 2. The primary end point of this study was the rate of postoperative complications, compared according to the modified Clavien-Dindo complication grading system. Observation indexes including postoperative fever, inflammation index change (postoperative blood leukocytes and neutrophils ratio changes value), hemorrhage (value changes of postoperative hemoglobin, red blood cell pressure change value and the incidence of renal subcapsular hematoma), kidney damage (postoperative serum creatinine values change), pain (VAS pain score, non-steroidal anti-inflammatory analgesic, and opioids demand rate) and the incidence of pleural effusion. Secondary end points included stone clearance rate, operation duration, postoperative hospital stay, and hospital costs. 3. Follow-up data included pain, hematuria, fever and readmission for 3 months after operation. Three researchers conducted data statistics respectively and obtained three original data, which were finally averaged.
19. **Statistical analysis plan**: SPSS26.0 version statistical software was used for analysis. Measurement data were expressed as mean ± standard deviation ($X \pm S$), and Student's t-test was used for intergroup comparisons. The counting data were expressed as frequency and percentage, and the chi-squared or

Fisher's exact probability test was used for intergroup comparisons. The ranksum test was used for grade data. $P<0.05$ was considered statistically significant.

20. **Approval of informed consent and ethics**: This study followed the ethical standards set out in the Declaration of Helsinki. Informed consent was obtained and signed by all enrolled patients to undergo the two surgical procedures (total tubeless PCNL without reverse insertion of a ureteral catheter and conventional total tubeless PCNL) and to collect and use the medical information and biological samples for the study.
21. **Confidentiality measures**: The identifiable information of the subjects is replaced by irrelevant character sequences to ensure that the relevant personal information of the subjects will not be disclosed in any form.
22. **Declaration of Interest**: There is no conflict of interest between the investigator and the organization.
23. **Data Acquisition**: When proper editing or review requirements are met, the study data may be obtained from the study manager after the study is completed.