



# Comparative Outcomes of One-Stage versus Two-Stage Percutaneous Nephrolithotomy: A National Population-Based Study on the Use of Shock Wave Lithotripsy for Residual Stones

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**Objective:** The objective of the study is to compare the rates of shock wave lithotripsy (SWL) treatment used for residual stones after one-stage versus two-stage percutaneous nephrolithotomy (PCNL).

**Methods:** This retrospective, national, population-based study was conducted using data from Taiwan's National Health Insurance Research Database between 2000 and 2017. The study divided PCNL participants into two cohorts. The 'one-stage cohort' had renal access created by urologists in the operating room immediately before PCNL. The 'two-stage cohort' involved radiologists creating this access in the angiography suite prior to the scheduled PCNL. Patients with prior SWL or missing data were excluded. Fine-Gray regression hazard models were used to calculate the subdistribution hazard ratio (sHR) for SWL occurrence between the two-stage and one-stage cohorts.

**Results:** Of the 36,253 patients who underwent PCNL within the study period, 17,964 were categorized into the one-stage cohort and 18,289 into the two-stage cohort. The one-stage cohort exhibited a lower rate of post-PCNL SWL than the two-stage cohort (2.25% vs. 2.9%,  $p = 0.0001$ ). After adjusting for age, gender, and comorbidities, the sHR for SWL in the two-stage cohort was 1.29 (95% confidence interval [CI], 1.13 – 1.47;  $p = 0.0001$ ). Furthermore, the one-stage cohort demonstrated lower admission costs than the two-stage cohort (NT\$63,396 ± 41,211 vs. NT\$78,295 ± 67,557,  $p < 0.0001$ ).

**Conclusions:** In this study, one-stage PCNL was associated with a lower subsequent SWL rate and lower admission costs than two-stage PCNL.

**Key words:** shock wave lithotripsy, one-stage percutaneous nephrolithotomy, two-stage percutaneous nephrolithotomy

## Introduction

Over the past four decades, percutaneous nephrolithotomy (PCNL) has evolved into the preferred treatment for renal stones

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larger than 2 cm because it can provide a higher stone-free rate, than ureteroscopy or shock wave lithotripsy (SWL), while offering a less invasive alternative to open or laparoscopic surgeries.<sup>1</sup>

Establishing percutaneous renal access is a critical initial step in PCNL because the quality of access can significantly impact the procedural outcomes and the risk of complications.<sup>2</sup> There are two methods for achieving percutaneous access for PCNL. First approach involves performing the procedure in the operating room just before the PCNL, a method known as ‘one-stage PCNL’. Second, percutaneous access can also be conducted by the radiologists in the angiography suite prior to the scheduled PCNL, known as ‘two-stage PCNL’. Recent studies have shown that less than 20% of patients undergoing PCNL have percutaneous renal access created by urologists.<sup>3,4</sup> Patients in whom renal access was created by urologists had lower complications than those in whom renal access was created by radiologists.<sup>3</sup> A previous investigation revealed that the total stone-free rate increased by 6.9% when urologists performed percutaneous renal access compared with radiologists (99% vs. 92.1%;  $p = 0.033$ ).<sup>5</sup>

Residual renal stones can remain after the PCNL procedure, which can lead to stone regrowth or urinary symptoms, such as urinary tract infections and blockage in the ureter.<sup>6,7</sup> Owing to these concerns, managing residual stones post-PCNL may be essential, with additional PCNL, SWL, and retrograde intrarenal surgery (RIRS) being effective treatment alternatives. A previous study comparing RIRS and SWL in addressing post-PCNL residual stones found that RIRS achieved a markedly higher stone-free rate than SWL (58.3% vs. 24.2%,  $p = 0.007$ ).<sup>8</sup> Despite the higher stone-free rate achieved by RIRS in treating post-PCNL residual stones, SWL maintains its relevance because of its distinct advantages as an outpatient and noninvasive treatment option for managing residual stone fragments fol-

lowing PCNL.<sup>9</sup> Studies have shown that stone location and comorbidities significantly affect the outcomes of SWL. Patients with one comorbidity had a 2.4 times higher likelihood of retaining residual stones than those without any comorbidity ( $p = 0.04$ ).<sup>10</sup>

We hypothesized that patients undergoing one-stage PCNL may require fewer subsequent SWL treatments for residual stones post-PCNL than patients who undergo two-stage PCNL. This could be because urologists create their own renal access with a better understanding of how to remove stones effectively and the ability to create additional tracts during surgery to handle complex stone cases.<sup>11</sup> The main objective of this study is to assess the rate of SWL treatment for residual stones after one-versus two-stage PCNL.

## Materials and Methods

### Data source and ethical considerations

The data used in this study were extracted from the claims records of Taiwan’s compulsory National Health Insurance (NHI) program. Managed by the Collaboration Center of Health Information Application (CCHIA) under the Ministry of Health and Welfare, the comprehensive NHI database covers over 99% of the population’s healthcare information, including demographic details, clinical visit dates, diagnostic codes, prescriptions, and associated costs. Disease coding during the study period was performed using International Classification of Diseases, Ninth and Tenth Revision, Clinical Modification.

The National Health Insurance Research Database (NHIRD) contains de-identified secondary data publicly available for research purposes. As such, this study was exempt from a full institutional review board evaluation.

### Study design and population

The study subjects were identified from the NHI-CCHIA database of patients who un-

derwent PCNL between 2000 and 2017. These PCNL cases were stratified into two cohorts: The “one-stage cohort” had urologists achieve renal access immediately prior to PCNL in the operating room, while the “two-stage cohort” involved radiologists first creating access in the angiography suite ahead of the scheduled PCNL procedure. The index date was defined as the date of PCNL in both cohorts. Patients who underwent SWL before the index PCNL date or those with missing data were excluded from the analysis.

### Comorbidities

Comorbidities identified as preexisting conditions included hypertension and gout, in addition to parameters of the Charlson Comorbidity Index (CCI), including myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic lung disease, connective tissue disease, ulcer, chronic liver disease, diabetes, diabetes with end-organ damage, hemiplegia, moderate or severe kidney disease, tumor, leukemia, lymphoma, moderate or severe liver disease, malignant tumor, metastasis, and acquired immunodeficiency syndrome (AIDS).

### Follow-up and outcomes

The follow-up period compared the outcomes between the two cohorts until SWL, health plan disenrollment/mortality, or one year after the index day.

### Statistical analysis

The baseline characteristics of the two cohorts were initially analyzed. Conventional survival analyses typically focus on a single event (e.g., death or SWL), potentially missing other events and overestimating risks. To address this, our study employed the Fine-Gray regression model to account for the competing risk of mortality when calculating the subdistribution hazard ratio (sHR) for SWL occurrence between cohorts, with *p*-values from Gray’s

test. A stratified Cox proportional hazard model was used to determine the hazard ratio (HR) of mortality for the two-stage versus one-stage cohorts. Sensitivity analyses across comorbidity subgroups using the Fine and Gray models were used to evaluate these assumptions. Data management, HR, and sHR calculations were performed using statistical analysis system (SAS) software for Windows (version 9.4; SAS Institute, Cary, NC), with the proportional hazards regression package for competing risk modeling.

## Results

### Cohort assembly

In this study, we selected 39,934 patients who underwent PCNL, between 2000 and 2017, from the NHI-CCHIA database. After excluding 194 patients with missing data and 1,748 patients who underwent SWL before the index day, 17,964 patients were classified into the one-stage cohort. Similarly, after excluding 212 patients with missing data and 1,527 patients who underwent SWL before the index day, 18,289 patients were included in the two-stage cohort. The enrollment process is illustrated in Figure 1.

### Baseline characteristics

Table 1 shows the baseline characteristics of the study participants. In the one-stage and two-stage cohorts, the mean age was  $55.05 \pm 12.69$  years, while in the two-stage cohort, it was  $55.42 \pm 12.42$  years. Patients in the two-stage cohort had a higher prevalence of diabetes (24.65% vs. 22.96%,  $p = 0.0002$ ), diabetes with end-organ damage (7.59% vs. 6.07%,  $p < 0.0001$ ), moderate or severe kidney disease (11.5% vs. 10.52%,  $p = 0.003$ ), and hypertension (52.42% vs. 50.6%,  $p = 0.0005$ ) than those in the one-stage cohort. Patients in the one-stage cohort demonstrated a lower SWL rate than those in the two-stage cohort (2.25% vs. 2.9%,  $p = 0.0001$ ). Furthermore, the

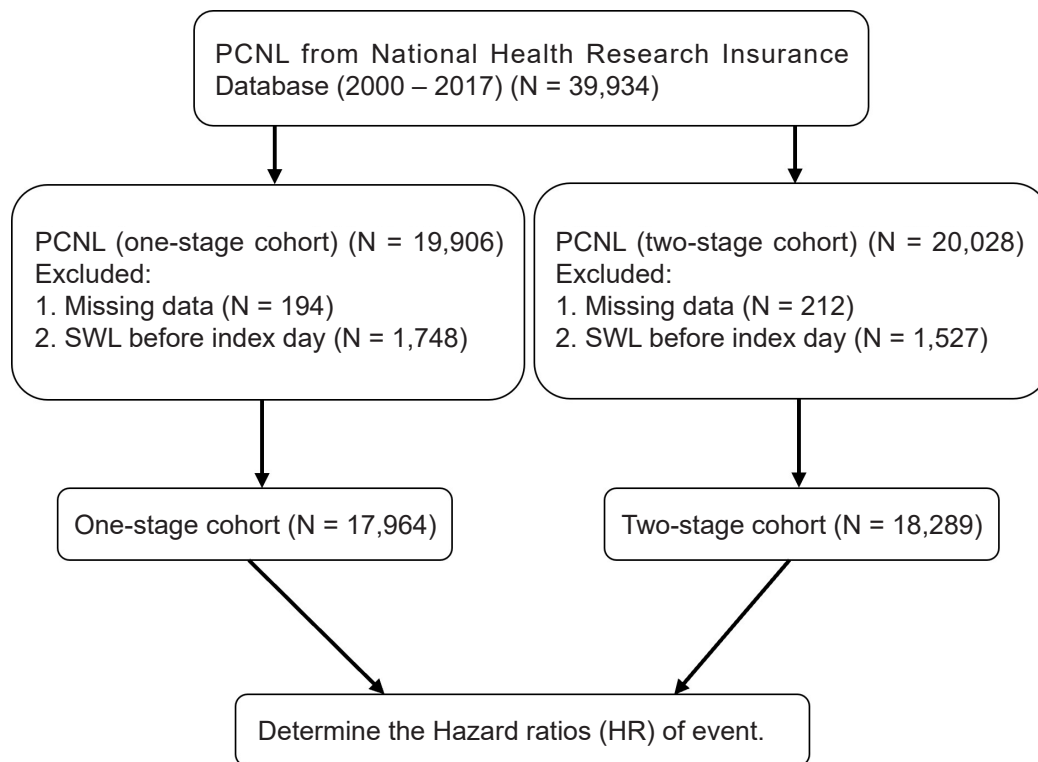


Fig. 1 Study flow. PCNL: percutaneous nephrolithotomy; SWL: shock wave lithotripsy.

two-stage cohort had higher admission costs (NT\$78,295 ± 67,557 vs. NT\$63,396 ± 41,211,  $p < 0.0001$ ) than one-stage cohort. Moreover, the analysis revealed that the one-year mortality showed no notable divergence between the two participant groups.

### Risk of SWL

Table 2 shows the predicted occurrence of SWL. The Fine and Gray regression hazards showed that the sHR of SWL occurrence for two-stage cohort was 1.29 (95% confidence interval [CI], 1.13 – 1.47;  $p = 0.0001$ ) compared to the one-stage cohort. After adjusting for gender, age, and comorbidities, the sHR for SWL occurrence for two-stage cohort was 1.29 (95% CI, 1.13 – 1.47;  $p = 0.0001$ ) compared to the one-stage cohort.

### Comorbidity-stratified analyses

Table 3 presents the adjusted HRs for SWL occurrence and mortality among patients who underwent PCNL in Taiwan between 2000

and 2017. Among patients with diabetes, the two-stage cohort experienced a higher sHR for SWL occurrence at 1.38 (95% CI: 1.07 – 1.79;  $p = 0.0122$ ) than the one-stage cohort. Similarly, patients with hypertension showed an increased sHR for SWL occurrence in the two-stage cohort at 1.24 (95% CI: 1.03 – 1.48;  $p = 0.0201$ ), and for patients with gout, the sHR for SWL occurrence was 1.60 (95% CI: 1.16 – 2.20;  $p = 0.0041$ ) when comparing the two-stage to the one-stage cohort.

### Mortality

Cox proportional hazards analysis, stratified by age, gender, and comorbidities, revealed that the adjusted HR for mortality in the two-stage cohort was 1.16 (95% CI, 1.01 – 1.34;  $p = 0.0406$ ) compared to the one-stage cohort.

### Discussion

Our study showed that patients undergoing one-stage PCNL were less likely to require

Table 1. Baseline characteristics of the study population.

|                                   | One-stage cohort<br>N = 17,964 | Two-stage cohort<br>N = 18,289 | p-value  |
|-----------------------------------|--------------------------------|--------------------------------|----------|
| Age (years)                       | 55.05 ± 12.69                  | 55.42 ± 12.42                  | 0.0055   |
| Gender                            |                                |                                | 0.1078   |
| Female                            | 6,526 (36.33)                  | 6,793 (37.14)                  |          |
| Male                              | 11,438 (63.67)                 | 11,496 (62.86)                 |          |
| Comorbidities                     |                                |                                |          |
| Myocardial infarct                | 566 (3.15)                     | 533 (2.91)                     | 0.1893   |
| Congestive heart failure          | 760 (4.23)                     | 749 (4.10)                     | 0.5189   |
| Peripheral vascular disease       | 401 (2.23)                     | 405 (2.21)                     | 0.9085   |
| Cerebrovascular disease           | 2,035 (11.33)                  | 2,055 (11.24)                  | 0.7820   |
| Dementia                          | 248 (1.38)                     | 232 (1.27)                     | 0.3509   |
| Chronic lung disease              | 4,036 (22.47)                  | 4,145 (22.66)                  | 0.6541   |
| Connective tissue disease         | 353 (1.97)                     | 339 (1.85)                     | 0.4380   |
| Ulcer                             | 5,554 (30.92)                  | 5,461 (29.86)                  | 0.0285   |
| Chronic liver disease             | 3,082 (17.16)                  | 3,131 (17.12)                  | 0.9256   |
| Diabetes                          | 4,124 (22.96)                  | 4,508 (24.65)                  | 0.0002   |
| Diabetes with end organ damage    | 1,091 (6.07)                   | 1,389 (7.59)                   | < 0.0001 |
| Hemiplegia                        | 341 (1.90)                     | 397 (2.17)                     | 0.0663   |
| Moderate or severe kidney disease | 1,890 (10.52)                  | 2,103 (11.50)                  | 0.0030   |
| Tumor, leukemia, lymphoma         | 1,212 (6.75)                   | 1,356 (7.41)                   | 0.0133   |
| Moderate or severe liver disease  | 88 (0.49)                      | 116 (0.63)                     | 0.0661   |
| Malignant tumor, metastasis       | 236 (1.31)                     | 212 (1.16)                     | 0.1829   |
| AIDS                              | 9 (0.05)                       | 5 (0.03)                       | 0.2701   |
| Hypertension                      | 9,090 (50.60)                  | 9,587 (52.42)                  | 0.0005   |
| Gout                              | 3,641 (20.27)                  | 3,731 (20.40)                  | 0.7550   |
| Admission costs (NT\$)            | 63,396 ± 41,211                | 78,295 ± 67,557                | < 0.0001 |
| SWL                               | 405 (2.25)                     | 530 (2.90)                     | 0.0001   |
| One-year mortality                | 367 (2.04)                     | 413 (2.26)                     | 0.1579   |

AIDS: acquired immunodeficiency syndrome; SWL: shock wave lithotripsy.

SWL for the treatment of residual stones than those undergoing two-stage PCNL, a trend that persisted even after adjusting for age, gender, and comorbidities. This finding provides urologists with increased confidence in performing one-stage PCNL, potentially reducing the need for SWL to treat residual stone fragments.

Despite urologists having the capability to perform percutaneous renal access, fewer than 20% had percutaneous renal access obtained by themselves.<sup>3,4</sup> However, most of these procedures are conducted by the radiologists. Lee *et al.* investigated why urologists often do not perform their own renal access.<sup>12</sup> They found that urologists who received renal access training during their residency were more likely to perform PCNL than those who did not. Furthermore, trained urologists were more

likely to perform their own renal access, with a higher rate compared to those untrained. They also found that the main reasons for urologists not performing their own access included better equipment available to radiologists (61%), extra time required for access (50%), and radiologists with better skills (44%). Additionally, De la Rosette *et al.* addressed the issue of few urologists performing access themselves, and recommended incorporating radiological access to the renal cavities into residency programs to improve this issue.<sup>13</sup>

Stone-free rates after post-PCNL show significant variation, ranging from 42% to 90%.<sup>7,14,15</sup> Previous studies have specifically explored the differences in stone-free rates between one- and two-stage PCNL.<sup>11,15-17</sup> Chen *et al.* observed no significant difference

Table 2. Prediction for occurrence of SWL.

|                                   | Crude              |          | Adjusted           |          |
|-----------------------------------|--------------------|----------|--------------------|----------|
|                                   | sHR                | p-value  | sHR                | p-value  |
| Two-stage vs. One-stage           | 1.29 (1.13 – 1.47) | 0.0001   | 1.29 (1.13 – 1.47) | 0.0001   |
| Age                               | 1.00 (0.99 – 1.00) | 0.1105   | 0.99 (0.99 – 1.00) | 0.0161   |
| Male vs. Female                   | 0.72 (0.63 – 0.82) | < 0.0001 | 0.74 (0.65 – 0.84) | < 0.0001 |
| Comorbidities                     |                    |          |                    |          |
| Myocardial infarct                | 0.64 (0.40 – 1.01) | 0.0578   | 0.65 (0.41 – 1.05) | 0.0798   |
| Congestive heart failure          | 0.97 (0.70 – 1.34) | 0.8419   | 0.98 (0.70 – 1.39) | 0.9305   |
| Peripheral vascular disease       | 0.82 (0.51 – 1.33) | 0.4178   | 0.81 (0.50 – 1.32) | 0.3957   |
| Cerebrovascular disease           | 1.24 (1.02 – 1.49) | 0.0280   | 1.24 (0.99 – 1.54) | 0.0562   |
| Dementia                          | 1.28 (0.77 – 2.14) | 0.3364   | 1.20 (0.71 – 2.05) | 0.4975   |
| Chronic lung disease              | 1.08 (0.93 – 1.26) | 0.2984   | 1.14 (0.97 – 1.34) | 0.1100   |
| Connective tissue disease         | 1.31 (0.86 – 1.98) | 0.2048   | 1.29 (0.85 – 1.95) | 0.2395   |
| Ulcer                             | 0.92 (0.80 – 1.06) | 0.2628   | 0.96 (0.82 – 1.11) | 0.5450   |
| Chronic liver disease             | 0.76 (0.63 – 0.91) | 0.0035   | 0.77 (0.64 – 0.94) | 0.0091   |
| Diabetes                          | 1.15 (0.99 – 1.33) | 0.0638   | 1.22 (1.03 – 1.44) | 0.0243   |
| Diabetes with end organ damage    | 1.04 (0.81 – 1.33) | 0.7651   | 0.92 (0.70 – 1.23) | 0.5854   |
| Hemiplegia                        | 1.64 (1.14 – 2.36) | 0.0078   | 1.45 (0.98 – 2.14) | 0.0634   |
| Moderate or severe kidney disease | 0.93 (0.75 – 1.15) | 0.5041   | 0.97 (0.78 – 1.21) | 0.8056   |
| Tumor, leukemia, lymphoma         | 0.69 (0.51 – 0.93) | 0.0146   | 0.66 (0.47 – 0.92) | 0.0141   |
| Moderate or severe liver disease  | 0.97 (0.40 – 2.34) | 0.9467   | 1.23 (0.51 – 2.99) | 0.6487   |
| Malignant tumor, metastasis       | 1.02 (0.56 – 1.85) | 0.9425   | 1.55 (0.79 – 3.01) | 0.1999   |
| AIDS                              | NA                 |          | NA                 |          |
| Hypertension                      | 1.00 (0.88 – 1.13) | 0.9479   | 1.01 (0.87 – 1.17) | 0.9224   |
| Gout                              | 0.81 (0.68 – 0.96) | 0.0137   | 0.87 (0.73 – 1.05) | 0.1427   |

SWL: shock wave lithotripsy; sHR: subdistribution hazard ratio; AIDS: acquired immunodeficiency syndrome.

Table 3. Adjusted hazard ratios for SWL occurrence and death among patients underwent PCNL in Taiwan between 2000 – 2017.

|                         | Case<br>(Two-stage/One-stage) | SWL                |         | Death                    |         |
|-------------------------|-------------------------------|--------------------|---------|--------------------------|---------|
|                         |                               | Adjusted sHR*      | p-value | Adjusted HR <sup>+</sup> | p-value |
| Two-stage vs. One-stage |                               |                    |         |                          |         |
| All patients            | 413/364                       | 1.29 (1.13 – 1.47) | 0.0001  | 1.16 (1.01 – 1.34)       | 0.0406  |
| Patients with DM        | 139/108                       | 1.38 (1.07 – 1.79) | 0.0122  | 1.27 (0.98 – 1.63)       | 0.0681  |
| Patients with HTN       | 267/231                       | 1.24 (1.03 – 1.48) | 0.0201  | 1.19 (1.00 – 1.42)       | 0.0563  |
| Patients with gout      | 99/81                         | 1.60 (1.16 – 2.20) | 0.0041  | 1.31 (0.97 – 1.77)       | 0.0745  |

\*Using Fine and Gray regression and adjustment are made for patient's age, gender and comorbidities.

<sup>+</sup>Using Cox proportional regression and adjustment are made for patient's age, gender and comorbidities.

SWL: shock wave lithotripsy; PCNL: percutaneous nephrolithotomy; DM: diabetes mellitus; HTN: hypertension; sHR: subdistribution hazard ratio; HR: hazard ratio.

between the stone-free rates of one- and two-stage PCNL in their study.<sup>16</sup> Furthermore, another study revealed that the stone-free rates were 83.4% for one-stage PCNL and 86.1% for two-stage PCNL, indicating that despite the more complex renal stones in the one-stage group, advancements in urologists' skills in primary access placement and management of multiple stones have made the stone-free

rates of one-stage PCNL comparable to those of two-stage PCNL.<sup>11</sup> Watterson *et al.* reported a higher stone-free rate for one-stage PCNL compared to two-stage, attributing this success to improved primary access placement and expertise in handling complex and larger stone burdens.<sup>17</sup> Similarly, another study supported the efficacy of one-stage PCNL, presenting a stone-free rate of 92.8% versus 50% for

two-stage PCNL.<sup>18</sup> This study also analyzed patients with staghorn stones, revealing a stone-free rate of 87% for one-stage PCNL compared to 36% for two-stage PCNL, suggesting the PCNL's superior effectiveness in complex cases. However, owing to the inherent limitations of the NHIRD, it was not possible to accurately determine the stone-free rates following PCNL in our study.

After PCNL, residual stone fragments may remain, necessitating further management to prevent stone regrowth or blockage of the ureter.<sup>6,7</sup> The methods for treating residual stones post-PCNL include PCNL, SWL, and RIRS. Previous studies indicated that 1.4% of patients required repeat PCNL and 6.7% required SWL for the treatment of residual stones after PCNL.<sup>18</sup> Furthermore, this study reported that the proportion of patients requiring SWL after one-stage PCNL was 3.9%, in contrast to 16.1% of those undergoing two-stage PCNL. Additionally, our research indicates that the occurrence rate of SWL after one-stage PCNL was lower than that after two-stage PCNL, which is consistent with findings from earlier research. Since 2009, RIRS has increasingly become the preferred method for treating residual stones after PCNL because of its ability to address multiple stones and provide clear visualization of the entire collecting system.<sup>19</sup> However, few studies have compared the efficacies of RIRS and SWL for the treatment of residual stones after PCNL. Alexandre *et al.*, in 2020, first revealed that RIRS achieved a significantly higher 58.3% stone-free rate compared to 24.2% than SWL for treating residual stone fragments post-PCNL.<sup>8</sup> Despite the superior stone-free rate offered by RIRS, SWL still plays a crucial role because of its noninvasive nature, suitability for outpatient procedures, and shorter hospitalization times than RIRS.<sup>8</sup> Patients undergoing repeat PCNL and RIRS were excluded from the analysis. The NHIRD lacks laterality information to determine whether subsequent PCNL

procedures were performed on the same side as the index PCNL and procedural claims do not consistently distinguish RIRS as a distinct modality. Future studies using primary institutional databases with detailed operative records are warranted to comprehensively evaluate post-PCNL management beyond SWL.

Speed *et al.* concluded that one-stage PCNL could have lower admission costs compared to two-stage PCNL.<sup>3</sup> The authors attributed the higher costs associated with two-stage PCNL to a variety of factors, such as the increased expenses related to the multistep approach, extended duration of hospitalization, and the possibility of redundant charges being levied. Our study's findings, indicating that the cost of two-stage PCNL was higher than that of one-stage PCNL, are in line with those of previous research. Notably, the choice between one- and two-stage PCNL is likely multifactorial (e.g., access training and experience, equipment availability, institutional practice patterns, and operative considerations), and these determinants may also influence stone clearance and subsequent retreatment decisions.

There are several limitations inherent to the NHIRD. First, this was a retrospective claims-based analysis, and was subject to coding errors and incomplete coding. Second, the NHIRD lacks key clinical and intraoperative details (e.g., stone size, location, configuration, stone-free status, access strategy, operative time, and standardized complication grading), which precludes the use of established PCNL complexity scores and limited adjustment for procedural complexity. Third, stone laterality and episode linkage are unavailable; therefore, post-PCNL SWL and repeat procedures cannot be definitively attributed to residual fragments from the index PCNL, and excluding patients with any prior SWL to define an index cohort may introduce selection effects. Fourth, provider-, facility-, and technique-level factors (e.g., operator experience, puncture technique, and hospital

volume), as well as heterogeneity in SWL devices and treatment parameters, were not captured and may have contributed to residual confounding. Finally, admission-level costs reflect the overall hospitalization expenditures, which may be influenced by comorbidities, intercurrent infections, and non-urological care, making it difficult to isolate PCNL-specific and postoperative urological costs. Future studies using institutional primary databases with imaging and laterality information as well as granular perioperative and cost data are warranted.

## Conclusions

In this study, one-stage PCNL was associated with lower subsequent SWL rates and lower admission costs than two-stage PCNL. These nationwide administrative data highlight the differences in retreatment utilization and hospitalization-level expenditures between the two strategies. Further studies using primary clinical databases with imaging-verified outcomes are required to validate these findings.

## Author Contributions

SHC: Project development, Data collection, and Manuscript writing; RCYW: Data analysis, and Manuscript editing.

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Health Insurance, Department of Health, or the National Health Research Institutes.

## Institutional Review Board Statement

This study was approved by the Institutional Review Board of the E-Da Hospital (EDAH IRB No. EMRP-108-061; approval date: July 20, 2019). The requirement for informed consent was waived by the IRB due to the retrospective nature of the study and the use of de-identified data. The study was conducted in accordance with the Declaration of Helsinki and relevant guidelines.

## Informed Consent Statement

As this study utilized de-identified secondary data from the NHIRD, managed by the CCHIA, Ministry of Health and Welfare, Taiwan, and the data is not publicly accessible, individual consent to participate was not required.

## Data Availability Statement

The data used in this study was sourced from the NHIRD, managed by the CCHIA, Ministry of Health and Welfare, Taiwan. The data is not publicly accessible. Access to this dataset requires approval from CCHIA, which includes submitting a research proposal and obtaining the necessary permissions. Data analysis can only be conducted at designated CCHIA locations (e.g., the National Cheng Kung University branch, Tainan City, Taiwan) during specified hours (Monday to Friday, 9:00 AM to 6:00 PM). Following analysis, only the resulting reports may be taken out, subject to further review by CCHIA. Due to privacy considerations, we are unable to provide a direct link to the database. Please note that we hold the rights to analyze the data but do not possess ownership of the dataset. Additional information regarding these regulations can be found at

<https://dep.mohw.gov.tw/DOS/cp-5119-59201-113.html>.

## Conflicts of Interest

The authors declare no conflict of interest.

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