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Contemporary Trends In Utilization And Perioperative Outcomes Of Percutaneous Nephrolithotomy In The United States From 2003 To 2014

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Running title: Contemporary PCNL trends and outcomes in the US

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ABSTRACT

Purpose: To investigate contemporary trends and perioperative outcomes of PCNL using a population-based cohort.

Materials and methods: Using the Premier Healthcare Database, we identified 225,321 patients diagnosed with kidney/ureter calculus who underwent PCNL at 447 different hospitals across the United States from 2003 to 2014. Outcomes included 90-day postoperative complications (as classified by the Clavien-Dindo system), prolonged hospital length of stay, operating room time, blood transfusions and direct hospital costs. Temporal trends were quantified by estimated annual percent change (EAPC) using least squares linear regression analysis. Multivariable logistic regression was performed to identify predictors of outcomes.

Results: PCNL utilization rates initially increased from 6.7% (2003) to 8.9% (2008) (EAPC +5.60%, p=0.02), before plateauing at 9.0% (2008-2011), then declining to 7.2% in 2014 (EAPC -4.37%, p=0.02). Overall (Clavien≥1) and major complication (Clavien≥3) rates rose significantly (EAPC: +12.2% and +16.4% respectively, both p<0.001). Overall/major complication and blood transfusion rates were 23.1%/4.8% and 3.3% respectively. Median operating room time and 90-day costs were 221 mins (IQR 4) and $12734 (IQR $9419), respectively. Significant predictors of overall complications include higher Charlson comorbidity index (CCI) (CCI≥2: OR 2.08, p<0.001) and more recent year of surgery (2007-2010: OR 3.20, 2011-2014: OR 4.39, both p<0.001). Higher surgeon volume was significantly associated with decreased overall (OR 0.992, p<0.001) and major (OR 0.991, p=0.01) complications.

Conclusions: Our contemporary analysis shows a decrease in utilization of PCNL in recent years, along with an increase in complication rates. Numerous patient, hospital and surgical characteristics affect complication rates.

Key words: percutaneous nephrolithotomy, complications, morbidity, kidney stones

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INTRODUCTION

The 2016 American Urological Association/Endourological Society guidelines recommend PCNL as first-line treatment for symptomatic patients with a total renal stone burden >20mm.[1, 2] Additionally, PCNL should be considered primary treatment for most cases with lower pole stones >10mm, however clinicians should inform patients that while PCNL has a higher stone-free rate, it confers a higher morbidity rate, compared to RIRS.

A recent article using the United States Nationwide Inpatient Sample described PCNL use from 1999 to 2011, noting its increase in utilization from 1.7/100,000 to 3.1/100,000.[3]. As for other modalities of stone treatment, a Canadian population-based study using administrative data found a rise in URS and reciprocal decrease in SWL for kidney stone treatment.[4]

Contemporary data has demonstrated that flexible URS is increasingly challenging PCNL in the treatment for medium to large sized kidney stones.[7-10] Despite this, PCNL remains the standard of care for kidney stones >2cm with continued improvements to techniques and approaches.[1, 2] A recent meta-analysis also found that standard PCNL conferred higher stone-free rates, albeit at the expense of higher complication rates, more blood loss and longer hospital stay, compared to RIRS.[11] Given that there exists limited updated data on contemporary utilization rates and outcomes of PCNL as well as costs associated with the procedure, we aimed to characterize national utilization trends, perioperative outcomes and costs using a contemporary population-based cohort.

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PATIENTS AND METHODS

Data source

After obtaining institutional review board waiver for use of anonymized HIPAA-compliant data, we utilized the Premier Healthcare Database (Premier, Inc., Charlotte, NC), a nationally representative all-payer database capturing over 75 million hospital inpatient discharges. It represents approximately 20% of all hospitalizations at over 700 hospitals in the US and features detailed information on a patient's hospitalization including demographics, hospital characteristics, and complete billing information. Apart from *International Classification of Diseases, Ninth Revision* (*ICD-9*), this claims-based database provides standardized billing items including direct item costs for all hospitalizations (e.g. medications, laboratory services, room and board, etc). This database has been featured in prior landmark studies.[12] Using validated projection methodology the data represents weighted estimates hospital admissions. All numbers reported herein refer to the weighted estimates.

Study Population

Using *ICD-9* codes, we identified individuals diagnosed with kidney or ureteric calculi (592.0, 592.1, 592.9) who underwent PCNL (55.04 or 55.03 combined with 55.21) between January 1, 2003 and December 31, 2014. Patients treated with PCNL were identified as previously described, using *ICD-9* procedural codes 55.04 for percutaneous nephrostomy with fragmentation and 55.03 for percutaneous nephrostomy combined with 55.21 for nephroscopy.[13]

Study Variables

We examined relevant patient, hospital, and surgical characteristics. Patient characteristics included age, gender (male vs. female), race (White vs. non-White), marital status (married vs. non-married), insurance status (Medicare, Medicaid, private/commerical, other), and

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Charlson Comorbidity Index (CCI) (0, 1, ≥2). Hospital characteristics included teaching status (teaching vs. non-teaching), size (<300, 300-499, ≥500 beds), urbanicity (urban vs. rural), annual hospital PCNL volume, and US geographic region (Midwest, Northeast, West, South). Surgical characteristics included annual surgeon PCNL volume and year of surgery (2003 to 2006, 2007 to 2010, 2011 to 2014). Hospital and surgeon volume were defined by the annual number of procedures undertaken by the hospital or surgeon in the year the procedure was undertaken for that particular patient. This gives the most current status of a hospital or surgeon's volume status.

Outcomes

We determined the rates of 90-day complication defined according to the Clavien-Dindo classification (Clavien 1-5) using ICD-9 codes as previously used.[14, 15] Prolonged LOS was defined as >75th percentile of LOS (>4 days) as previously done.[13] We also evaluated operating room time (which referred to the total length of procedure from the time the patient is brought into the operating room till the time the patient leaves – "wheels in, wheels out"), and receipt of intra- or post-operative blood transfusion. Use of post-operative vasopressors and admission to the ICU was determined using billing codes. Lastly, we calculated 90-day direct hospital costs, which included the cost of the entire procedure, inpatient stay, and any care up to 90-days postoperatively. All costs were adjusted to 2016 US dollars using the medical component of the Consumer Price Index.

Statistical Analyses

For incidence of PCNL each year, we normalized this to population estimates from the latest 2014 US Census Bureau (for years 2010-2014) and from intercensus estimates (for years 2003-2009). Temporal trends in rates were analyzed by estimated annual percentage change (EAPC), which uses the least squares linear regression methodology. Next, we performed univariable analysis to evaluate outcomes. Categorical variables were summarized as proportions while continuous variables were expressed as means (with standard errors) and medians (with interquartile ranges).

Finally, we assessed patient-, hospital- and surgical-related predictors of outcomes. We developed a multivariable logistic regression model controlling for all covariates in order to assess for independent predictors of outcomes, as listed above. 90-day direct hospital costs were found to have a gamma distribution, so we constructed generalized linear regression models. All statistical analyses were performed using SAS 9.3 (SAS Institute, NC). All tests were two-sided and a p-value of <0.05 was considered statistically significant.

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RESULTS

Our final cohort consisted of a weighted sample of 225,321 patients who underwent PCNL by 3311 unique surgeons at 447 different hospitals across the United States from 2003 to 2014. Baseline characteristics are listed in **Table 1**. Temporal trends analysis showed a non-significant overall increase in annual percentage of PCNL being performed (EAPC: +1.1%, 95% CI: -0.87% to +3.12%, p= 0.24), with an initial increase from 6.7% in 2003 to 8.9% in 2008 (EAPC +5.60%, 95% CI: 1.31% to 10.1%, p= 0.02), before plateauing between 2008 to 2011 at 8.9-9.0%, then significantly declining to 7.2% in 2014 (EAPC: -4.37%, 95% CI: -7.27% to -1.37%, p=0.02). The overall incidence of PCNL performed annualized to the US population was 5.49/100,000 in 2003 and declined to 5.34/100,000 in 2014. Similar trends are noted when examining males and females separately (**Figure 1**). There is an increasing trend in age and proportion of patients with poorer CCI (**Figure 2**).

Overall complication rates saw an increasing trend from 6.6% in 2003 to 33.1% in 2014 (EAPC +12.2%, 95% CI: 6.63% to 18.07%); this was similar for major complication rates, from 0.4% in 2003 to 8.6% in 2014 (EAPC +16.4%, 95% CI: 6.94% to 26.60%; both p<0.001) (**Figure 3**). Overall and major complication rates were 23.1% and 4.8% during the study period. Median hospital LOS was 2.47 (IQR 3.09) days, with 28.0% of patients having a prolonged LOS (>4 days). A minority (3.2%) of patients required postoperative ICU admission, with use of vasopressors post-operatively at 5.3%. Trends in selected outcomes were graphed on **Figure 3.** Median operating room time was 159 (IQR 90) minutes. Median 90-day direct hospital costs were $12,734 (IQR: $9419) (**Table 2**).

Predictors of overall complications

Multivariable logistic regression identified the following significant predictors of overall complications: poorer CCI (vs. CCI 0, CCI 2: OR 2.08, 95% CI: 1.94-2.24, p<0.001), and recent year of surgery (vs. 2003-2006, 2007-2010: OR 3.20, 95% CI: 2.92-3.50; 2011-2014: OR 4.39, 95% CI: 4.01-4.80, both p<0.001). Higher surgeon volume was significantly associated with lower overall complications (OR 0.992, 95% CI: 0.988-0.997, p<0.001). Other predictors are listed in **Table 3**.

Predictors of major complications

On multivariable logistic regression, we found increasing age was a significant predictor of major complications (OR 1.004, 95% CI: 1.001-1.008, p=0.02) (**Table 3**). Other significant predictors of major complications include female gender (vs. male, OR 1.46, 95% CI: 1.31-1.62, p<0.001), non-married status (vs. married, OR 1.26, 95% CI: 1.13-1.42, p<0.001), Medicaid insurance status (vs. Medicare, OR 1.79, 95% CI: 1.50-2.13, p<0.001), higher CCI (vs. CCI 0, CCI 1: 1.66, 95% CI: 1.41-1.95; CCI 2: OR 3.10, 95% CI: 2.67-3.60, both p<0.001) and more recent year of surgery (vs. 2003-2006, 2007-2010: OR 2.29, 95% CI: 1.95-2.70; 2011-2014: OR 3.32, 95% CI: 2.83-3.89, both p<0.001). Higher hospital volume was also associated with major complications (OR 1.008, 95% CI: 1.005-1.012, p<0.001), while higher surgeon volume was associated with decreased major complications (OR 0.991, 95% CI: 0.984-0.998, p=0.01).

Predictors of prolonged LOS and 90-day direct hospital costs are listed in **Table 3.**

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DISCUSSION

We utilized a large population-based all-payer discharge database to evaluate trends and outcomes of patients who underwent PCNL in the United States from 2003 to 2014. To the best of our knowledge, this study is the largest cohort of PCNL patients (N=225,321), providing contemporary trends in its utilization and outcomes. During the study period, we found the utilization of PCNL had initially increased to a peak of 6.97/100,000 in 2008, before decreasing gradually to 3.63/100,000 in 2014. The rise in incidence was congruent with findings from Stern *et al*., who used the Nationwide Inpatient Sample from 1999 to 2011 (N=105,180).[3] However, our findings of the subsequent decrease in incidence of PCNL from 2008 to 2014 are new and noteworthy. Recent data had demonstrated an important increase in the use of URS over the past 10 years with a similar decrease in the use of SWL.[4-6] Over this same time frame PCNL utilization remained stable. Contemporary data is now demonstrating that URS is not only having an impact on the utilization of SWL but it may also affect the utilization of PCNL. It would appear that RIRS is beginning to selectively decrease the number of PCNL cases that are being performed in the United States.

Similarly, we found an overall increase in overall and major complication rates across the study period. This may be due to the medium-sized stones being increasingly managed with flexible URS,[11, 16, 17] leaving the larger and/or more complex staghorn cases to be managed with PCNL. Another possibility that can account for the higher rates of complications is the increasing age and proportion of patients with more medical problems (as indicated by higher CCI) across the study period. As such, it was not unexpected to find that poorer CCI was a significant predictor of overall and major complications. Patients with CCI ≥2 had over twice the odds of developing postoperative complications and over 3 times the odds of developing major complications after PCNL. This suggests the importance of careful patient selection for PCNL. It remains to be seen whether patients with poor CCI might benefit from staged flexible URS procedure instead of a more morbid PCNL procedure.[18] Interestingly, at the beginning of our study period, complications rates

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(6-11%) were quite low. During this early time frame, it is plausible that flexible URS had not been widely adopted by most urologists and consequently, simple and smaller stones were still being managed by PCNL. A recent review of nephrolithometric scoring systems found that patients with Grade I-II Guy's stone score treated by PCNL had complication rates up to 10%.[19]

Through use of billing codes, we were also able to determine for the first-time a population-based rate of postoperative ICU admission at 3.2%. This was similar to the 3-4% rate found in a 2002-2006 study using the Truven Health's MarketScan Database, which was limited to working-age adults and their dependents with employer-sponsored benefit plans [20].

Another interesting finding relates to that of surgical volume. We were able to evaluate both annual hospital and surgeon volume. Higher hospital volume was significantly associated with more overall and major complications. While counterintuitive, this may be secondary to more complex cases being referred to higher volume hospitals.[21]. A study using the NIS found that complication and transfusion rates varied by case volume in a non-linear fashion, wherein rates were highest at the lowest and highest volume centers.[22]

In contrast, we found that higher surgeon volume was significantly associated with decreased overall and major complications, as well as decreased prolonged LOS. Notably we were able to determine complications according to the recommended Clavien-Dindo classification system.[23] A 2012 CROES PCNL study found higher stone-free rates and lower complication rates at high-volume centers, among 3933 patients, even after adjusting for important clinical variables like stone burden, urine culture status, ASA score, and the presence of staghorn stones.[24] Another nationwide study in Taiwan found higher surgeon volume was associated with lower medical costs and shorter LOS after PCNL, but surgeon

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volume did not predict complications or mortality.[25] Our study did not find a significant decrease in direct hospital costs with higher hospital (p=0.99) or surgeon volume (p=0.10).

Our study is not devoid of limitations. Firstly, this was a retrospective study using an administrative discharge database, therefore can be subject to misclassification bias. Secondly, we lacked important clinical information such as the location or size of the kidney stones, stone complexity grading systems (e.g. CROES nomogram[26, 27]), preoperative urine culture status, ASA score, or postoperative stone-free rates. From a list of 15 recommended outcomes to report for PCNL studies,[28] our study was able to report 5 outcomes (LOS, overall complication rate, operating time, blood transfusion, and cost). Thirdly, we were not able to determine what type of PCNLs was actually performed, i.e. supine vs. prone,[29] standard vs. mini vs. ultra-mini vs. micro.[30] Additionally, we could not evaluate patients who underwent flexible URS, RIRS or SWL, as these are usually day surgery cases, which would not require overnight hospitalization; hence we cannot draw any firm conclusions about trends in their use in comparison to PCNL. Lastly, this study is primary based on clinical practice and costs in the United States and may not reflect that in other parts of the world.

CONCLUSIONS

This large contemporary population-based study provides new insight into trends of utilization and outcomes of PCNL in the United States. We found an initial increase in utilization of PCNL during the earlier study period with a subsequent decrease in the more recent era. Contemporary decrease in utilization of PCNL may be due to an increase in the use of flexible URS. Additionally, increasing age, poorer comorbidity status, and possibly increasing complex cases being managed with PCNL may contribute to the rise in complication rates. Surgeon volume is an important factor in decreasing overall and major complications, as well as prolonged LOS. A variety of patient, hospital, and surgical related characteristics have been found to affect outcomes and may have implications on referral patterns and patient selection.

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REFERENCES

1. Assimos D, Krambeck A, Miller NL, et al. Surgical Management of Stones: American Urological Association/Endourological Society Guideline, PART I. The Journal of urology. 2016 Oct;196(4):1153-60. PubMed PMID: 27238616.

2. Assimos D, Krambeck A, Miller NL, et al. Surgical Management of Stones: American Urological Association/Endourological Society Guideline, PART II. The Journal of urology. 2016 Oct;196(4):1161-9. PubMed PMID: 27238615.

3. Stern KL, Tyson MD, Abdul-Muhsin HM, Humphreys MR. Contemporary Trends in Percutaneous Nephrolithotomy in the United States: 1998-2011. Urology. 2016 May;91:41-5. PubMed PMID: 26919962.

4. Ordon M, Urbach D, Mamdani M, Saskin R, RJ DAH, Pace KT. The surgical management of kidney stone disease: a population based time series analysis. The Journal of urology. 2014 Nov;192(5):1450-6. PubMed PMID: 24866599.

5. Turney BW, Reynard JM, Noble JG, Keoghane SR. Trends in urological stone disease. BJU international. 2012 Apr;109(7):1082-7. PubMed PMID: 21883851.

6. Heers H, Turney BW. Trends in urological stone disease: a 5-year update of hospital episode statistics. BJU international. 2016 Nov;118(5):785-9. PubMed PMID: 27128735.

7. Breda A, Ogunyemi O, Leppert JT, Schulam PG. Flexible ureteroscopy and laser lithotripsy for multiple unilateral intrarenal stones. European urology. 2009 May;55(5):1190-6. PubMed PMID: 18571315.

8. Breda A, Ogunyemi O, Leppert JT, Lam JS, Schulam PG. Flexible ureteroscopy and laser lithotripsy for single intrarenal stones 2 cm or greater--is this the new frontier? The Journal of urology. 2008 Mar;179(3):981-4. PubMed PMID: 18207179.

9. Mariani AJ. Combined electrohydraulic and holmium:YAG laser ureteroscopic nephrolithotripsy of large (greater than 4 cm) renal calculi. The Journal of urology. 2007 Jan;177(1):168-73; discussion73. PubMed PMID: 17162030.

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Journal of Endourology
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10. Wilhelm K, Hein S, Adams F, Schlager D, Miernik A, Schoenthaler M. Ultra-mini PCNL versus flexible ureteroscopy: a matched analysis of analgesic consumption and treatment-related patient satisfaction in patients with renal stones 10-35 mm. World journal of urology. 2015 Dec;33(12):2131-6. PubMed PMID: 25971205.

11. De S, Autorino R, Kim FJ, et al. Percutaneous nephrolithotomy versus retrograde intrarenal surgery: a systematic review and meta-analysis. European urology. 2015 Jan;67(1):125-37. PubMed PMID: 25064687.

12. Lindenauer PK, Pekow P, Wang K, Mamidi DK, Gutierrez B, Benjamin EM. Perioperative beta-blocker therapy and mortality after major noncardiac surgery. The New England journal of medicine. 2005 Jul 28;353(4):349-61. PubMed PMID: 16049209.

13. Ghani KR, Sammon JD, Bhojani N, et al. Trends in percutaneous nephrolithotomy use and outcomes in the United States. The Journal of urology. 2013 Aug;190(2):558-64. PubMed PMID: 23434944.

14. Leow JJ, Chang SL, Meyer CP, et al. Robot-assisted Versus Open Radical Prostatectomy: A Contemporary Analysis of an All-payer Discharge Database. European urology. 2016 Nov;70(5):837-45. PubMed PMID: 26874806.

15. Varda BK, Johnson EK, Clark C, Chung BI, Nelson CP, Chang SL. National trends of perioperative outcomes and costs for open, laparoscopic and robotic pediatric pyeloplasty. The Journal of urology. 2014 Apr;191(4):1090-5. PubMed PMID: 24513164. Pubmed Central PMCID: PMC4154938.

16. de la Rosette J, Denstedt J, Geavlete P, et al. The clinical research office of the endourological society ureteroscopy global study: indications, complications, and outcomes in 11,885 patients. Journal of endourology / Endourological Society. 2014 Feb;28(2):131-9. PubMed PMID: 24147820.

17. Giusti G, Proietti S, Villa L, et al. Current Standard Technique for Modern Flexible Ureteroscopy: Tips and Tricks. European urology. 2016 Jul;70(1):188-94. PubMed PMID: 27086502.

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18. Karakoyunlu N, Goktug G, Sener NC, et al. A comparison of standard PCNL and staged retrograde FURS in pelvis stones over 2 cm in diameter: a prospective randomized study. Urolithiasis. 2015 Jun;43(3):283-7. PubMed PMID: 25838180.

19. Vernez SL, Okhunov Z, Motamedinia P, Bird V, Okeke Z, Smith A. Nephrolithometric Scoring Systems to Predict Outcomes of Percutaneous Nephrolithotomy. Reviews in urology. 2016;18(1):15-27. PubMed PMID: 27162508. Pubmed Central PMCID: PMC4859924.

20. Alruwaily AF, Eisner BH, Bierlein MJ, et al. Statin Use and Risk of Sepsis After Percutaneous Nephrolithotomy. Journal of endourology / Endourological Society. 2015 Oct;29(10):1126-30. PubMed PMID: 25919429.

21. Morris DS, Taub DA, Wei JT, Dunn RL, Wolf JS, Jr., Hollenbeck BK. Regionalization of percutaneous nephrolithotomy: evidence for the increasing burden of care on tertiary centers. The Journal of urology. 2006 Jul;176(1):242-6; discussion 6. PubMed PMID: 16753409.

22. Kadlec AO, Ellimoottil C, Guo R, Trinh QD, Sun M, Turk TM. Contemporary volume-outcome relationships for percutaneous nephrolithotomy: results from the Nationwide Inpatient Sample. Journal of endourology / Endourological Society. 2013 Sep;27(9):1107-13. PubMed PMID: 23718230.

23. Mitropoulos D, Artibani W, Graefen M, et al. Reporting and grading of complications after urologic surgical procedures: an ad hoc EAU guidelines panel assessment and recommendations. European urology. 2012 Feb;61(2):341-9. PubMed PMID: 22074761.

24. Opondo D, Tefekli A, Esen T, et al. Impact of case volumes on the outcomes of percutaneous nephrolithotomy. European urology. 2012 Dec;62(6):1181-7. PubMed PMID: 22440402.

25. Huang WY, Wu SC, Chen YF, Lan CF, Hsieh JT, Huang KH. Surgeon volume for percutaneous nephrolithotomy is associated with medical costs and length of hospital stay: a nationwide population-based study in Taiwan. Journal of endourology / Endourological Society. 2014 Aug;28(8):915-21. PubMed PMID: 24707828.

26. Sfoungaristos S, Gofrit ON, Yutkin V, Landau EH, Pode D, Duvdevani M. External Validation of CROES Nephrolithometry as a Preoperative Predictive System for Percutaneous Nephrolithotomy Outcomes. The Journal of urology. 2016 Feb;195(2):372-6. PubMed PMID: 26316372.

27. Smith A, Averch TD, Shahrour K, et al. A nephrolithometric nomogram to predict treatment success of percutaneous nephrolithotomy. The Journal of urology. 2013 Jul;190(1):149-56. PubMed PMID: 23353048.

28. Opondo D, Gravas S, Joyce A, et al. Standardization of patient outcomes reporting in percutaneous nephrolithotomy. Journal of endourology / Endourological Society. 2014 Jul;28(7):767-74. PubMed PMID: 24571713.

29. Duty B, Okhunov Z, Smith A, Okeke Z. The debate over percutaneous nephrolithotomy positioning: a comprehensive review. The Journal of urology. 2011 Jul;186(1):20-5. PubMed PMID: 21571342.

30. Datta SN, Solanki R, Desai J. Prospective Outcomes of Ultra Mini Percutaneous Nephrolithotomy: A Consecutive Cohort Study. The Journal of urology. 2016 Mar;195(3):741-6. PubMed PMID: 26476354.

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DISCLOSURES

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KEY OF DEFINITIONS FOR ABBREVIATIONS

PCNL – percutaneous nephrolithotomy

RIRS – retrograde intra-renal surgery

URS – ureterorenoscopy

SWL – shockwave lithotripsy

EAPC – estimated annual percentage change

CROES – Clinical Research Office of the Endourological Society

ASA – American Society of Anesthesiologists

ICU – intensive care unit

LOS – length of stay

SE – standard errors

IQR – inter-quartile range

TABLES

Table 1. Baseline Characteristics Of Patients Who Underwent PCNL From The Premier Healthcare Database In The United States From 2003 To 2014

Patient characteristics	n	%
Mean age (s.e.)	55.1	0.10
Gender		
Male	106126	47.1%
Female	119195	52.9%
Race		
White	167177	74.2%
Non-White	58144	25.8%
Marital status		
Married	98377	43.7%
Non-married	126944	56.3%
Insurance status		
Medicare	94597	42.0%
Medicaid	26789	11.9%
Private	86558	38.4%
Other	17377	7.7%
Charlson comorbidity score		
0	108474	48.1%

1	52232	23.2%
≥2	64614	28.7%
Hospital characteristics		
Hospital teaching status		
Teaching	78447	34.8%
Non-teaching	146874	65.2%
Hospital bed size		
<300 beds	57674	25.6%
300-499 beds	98391	43.7%
≥500 beds	69256	30.7%
Hospital location		
Urban	216617	96.1%
Rural	8704	3.9%
Hospital region		
Midwest	55050	24.4%
Northeast	45938	20.4%
South	90135	40.0%
West	34198	15.2%
Hospital volume		
Mean annual volume (s.e.)	13.2	0.07
Surgical characteristics		
Surgeon volume		

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Mean annual volume (s.e.)	4.5	0.03
Year of surgery		
2003-2006	68448	30.4%
2007-2010	80938	35.9%
2011-2014	75935	33.7%

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Table 2. Outcomes Of Patients Who Underwent PCNL From The Premier Healthcare Database In The United States From 2003 To 2014

Outcomes	n	%
90-day postoperative complications		
Clavien 0 (no complications)	173233	76.9%
Clavien 1	21707	9.6%
Clavien 2	19522	8.7%
Clavien 3a	6.332	0.0%
Clavien 3b	31.172	0.0%
Clavien 4a	3234	1.4%
Clavien 4	7192	3.2%
Clavien 5 (mortality)	394.834	0.2%
Any Complication (Clavien ≥1)	52088	23.1%
Major Complication (Clavien ≥3)	10858	4.8%
Hospital length of stay		
Prolonged LOS (>75th percentile/>4 days)	63139	28.0%
Mean LOS (se)	4.62	0.03
Median LOS (IQR)	2.47	3.09
Intensive care unit (ICU)		
No	229306	96.8%
Yes	7694	3.2%

Mean LOS in ICU (se)	3.48	0.10
Use of vasopressors		
No	224432	94.7%
Yes	12567	5.3%
Mean no. of days using vasopressors (se)	1.27	0.02
Operating room time (mins)		
Mean time (se)	220.6	4.2
Median time (IQR)	159.0	90.0
Intra- or post-operative receipt of blood transfusion		
Received blood transfusion	7470	3.3%
Mean no. of units of blood products (se)	0.12	0.004
90-day direct hospital costs (2016 US$)		
Mean costs (se)	16571	79
Median costs (IQR)	12734	9419

Abbreviations: se (standard error), IQR (interquartile range)

** Mean ICU LOS was calculated from only among those who were admitted to ICU. Patients who did not require an ICU stay (i.e. ICU LOS = 0 days) were excluded from this calculation. Similarly, mean no. of days using vasopressors was calculated from only among those who required postoperative use of vasopressors. Those who did not have any postoperative use of vasopressors were excluded.*

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Table 3. Predictors of 90-Day Overall (Clavien≥1), Major (Clavien≥3) Complications, Prolonged Length of Stay, and 90-Day Direct Hospital Costs For Patient Undergoing PCNL in the United States (2003 to 2014)

	Overall (Clavien≥1) Complications				Major (Clavien≥3) Complications				Prolonged LOS (>75th percentile, i.e. >4 days)				90-Day Direct Hospital Costs (2016 US$)			
Patient characteristics	**Odds Ratio**	**95% Confidence Intervals**		**p value**	**Odds Ratio**	**95% Confidence Intervals**		**p value**	**Odds Ratio**	**95% Confidence Intervals**		**p value**	**Beta-coefficient**	**95% Confidence Intervals**		**p value**
Age	0.991	0.989	0.993	<0.001	1.004	1.001	1.008	0.02	0.988	0.986	0.990	<0.001	-50	-79	-22	<0.01
Gender																
Male	Ref				Ref				Ref				Ref			
Female	1.04	0.98	1.10	0.20	1.46	1.31	1.62	<0.001	1.07	1.01	1.14	0.02	494	-194	1182	0.16
Race																
White	Ref				Ref				Ref				Ref			
Non-White	0.90	0.84	0.96	<0.01	1.00	0.88	1.13	0.95	1.18	1.10	1.26	<0.001	324	-804	1452	0.57
Marital status																
Married	Ref				Ref								Ref			

Non-married	1.07	1.01	1.14	0.03	1.26	1.13	1.42	<0.001	1.33	1.25	1.42	<0.001	438	-371	1247	0.29
Insurance status																
Medicare	Ref				Ref				Ref				Ref			
Medicaid	0.91	0.82	1.02	0.09	1.79	1.50	2.13	<0.001	0.69	0.63	0.77	<0.001	-2062	-3684	-441	0.01
Private	0.69	0.64	0.74	<0.001	0.76	0.66	0.88	<0.01	0.45	0.41	0.48	<0.001	-3613	-4692	-2533	<0.01
Other	0.70	0.62	0.80	<0.001	0.72	0.55	0.94	0.02	0.51	0.45	0.58	<0.001	-3788	-5137	-2440	<0.01
Charlson comorbidity index																
0	Ref				Ref				Ref				Ref			
1	1.06	0.98	1.15	0.13	1.66	1.41	1.95	<0.001	1.15	1.07	1.24	<0.01	889	-27	1804	0.06
≥2	2.08	1.94	2.24	<0.001	3.10	2.67	3.60	<0.001	2.14	2.00	2.29	<0.001	3917	2606	5229	<0.01
Hospital characteristics																
Hospital teaching status																
Teaching	Ref				Ref				Ref				Ref			
Non-teaching	0.89	0.83	0.95	<0.01	0.62	0.55	0.70	<0.001	1.07	1.00	1.14	0.05	-951	-2281	379	0.16
Hospital bed size																
<300 beds	Ref				Ref				Ref				Ref			

300-499 beds	1.07	0.99	1.16	0.08	0.85	0.73	0.98	0.03	1.22	1.13	1.32	<0.001	232	-1348	1813	0.77
≥500 beds	1.08	1.00	1.18	0.06	0.91	0.79	1.06	0.23	1.59	1.46	1.72	<0.001	2309	397	4222	0.02
Hospital location																
Urban	Ref				Ref				Ref				Ref			
Rural	0.91	0.77	1.09	0.31	1.11	0.85	1.45	0.44	1.36	1.19	1.55	<0.001	2451	-182	5083	0.07
Hospital region																
Midwest	Ref				Ref				Ref				Ref			
Northeast	0.86	0.79	0.95	<0.01	0.65	0.56	0.75	<0.001	1.77	1.61	1.94	<0.001	1767	-881	4416	0.19
South	0.94	0.87	1.02	0.14	0.65	0.57	0.75	<0.001	1.26	1.16	1.37	<0.001	-1240	-3010	529	0.17
West	0.99	0.89	1.10	0.84	0.70	0.58	0.86	<0.01	1.13	1.01	1.25	0.03	1332	-749	3414	0.21
Hospital volume	1.003	1.001	1.004	0.01	1.008	1.005	1.012	<0.001	1.001	0.999	1.003	0.19	0	-40	40	0.99
Surgical characteristics																
Surgeon volume	0.992	0.988	0.997	<0.01	0.991	0.984	0.998	0.01	0.954	0.947	0.960	<0.001	-60	-131	11	0.10
Year of surgery																
2003-2006	Ref				Ref				Ref				Ref			
2007-2010	3.20	2.92	3.50	<0.001	2.29	1.95	2.70	<0.001	1.11	1.03	1.19	0.01	1249	89	2410	0.04

2011-2014	4.39	4.01	4.80	<0.001	3.32	2.83	3.89	<0.001	0.87	0.81	0.93	<0.01	-534	-1716	648	0.38

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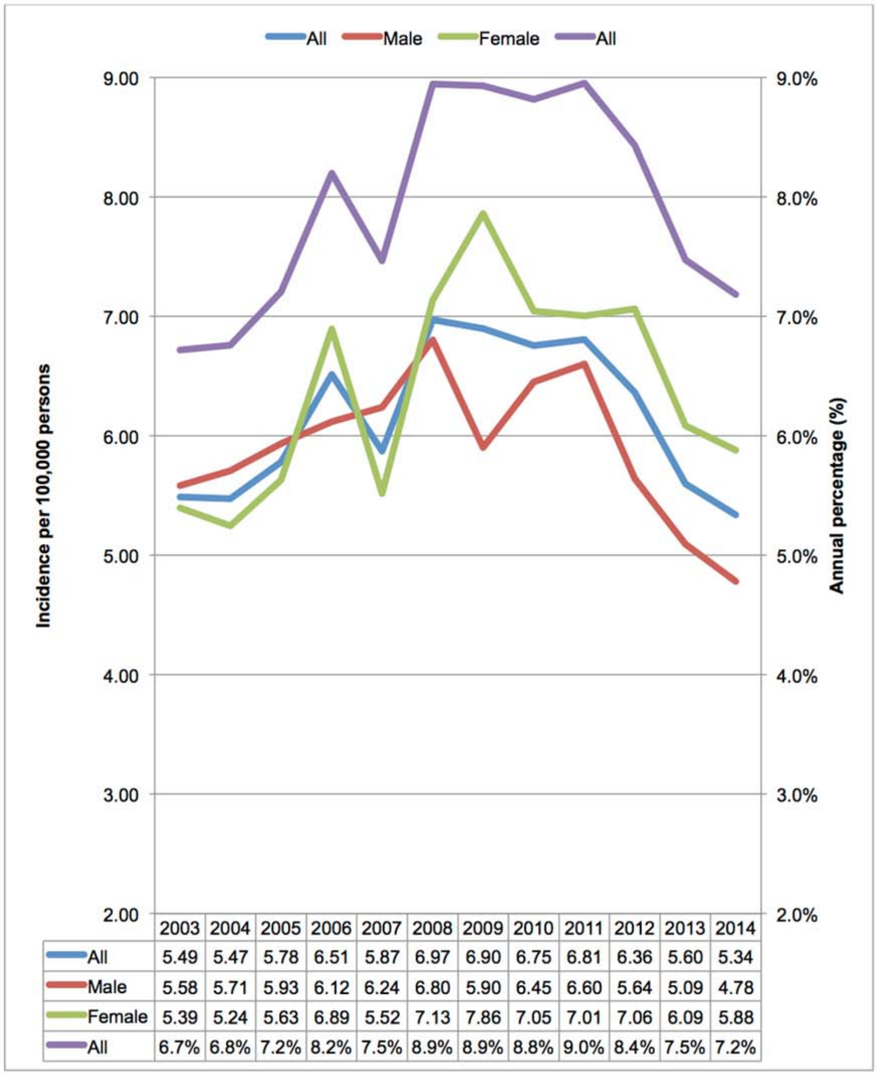
FIGURE LEGENDS

Figure 1.



	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
All	5.49	5.47	5.78	6.51	5.87	6.97	6.90	6.75	6.81	6.36	5.60	5.34
Male	5.58	5.71	5.93	6.12	6.24	6.80	5.90	6.45	6.60	5.64	5.09	4.78
Female	5.39	5.24	5.63	6.89	5.52	7.13	7.86	7.05	7.01	7.06	6.09	5.88
All	6.7%	6.8%	7.2%	8.2%	7.5%	8.9%	8.9%	8.8%	9.0%	8.4%	7.5%	7.2%

Figure 1. Trend In Incidence Of PCNL Hospitalization (From Premier Healthcare Database) In The United States From 2003 To 2014

Figure 2.

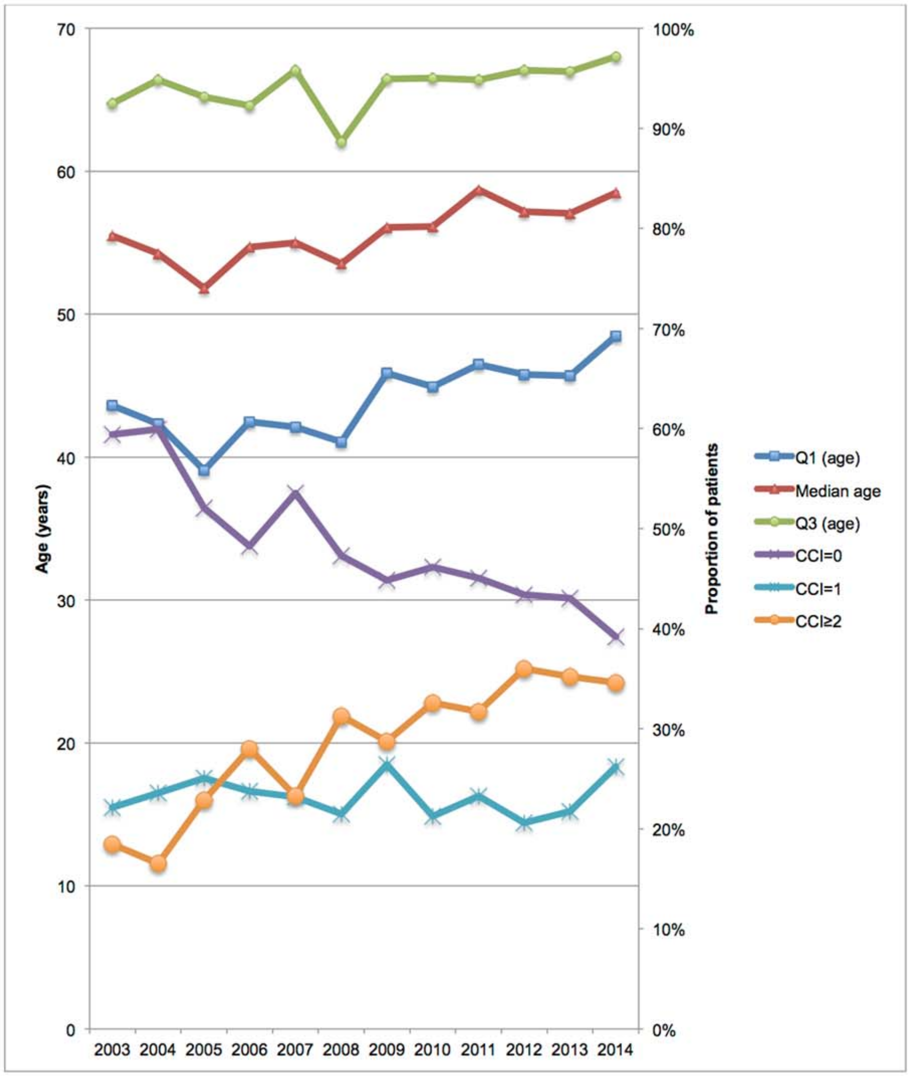


Figure 2. Trend of Median Age (Interquartile Range) and Charlson Comorbidity Index of Patients Who Underwent PCNL From The Premier Healthcare Database In The United States From 2003 To 2014

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Figure 3.

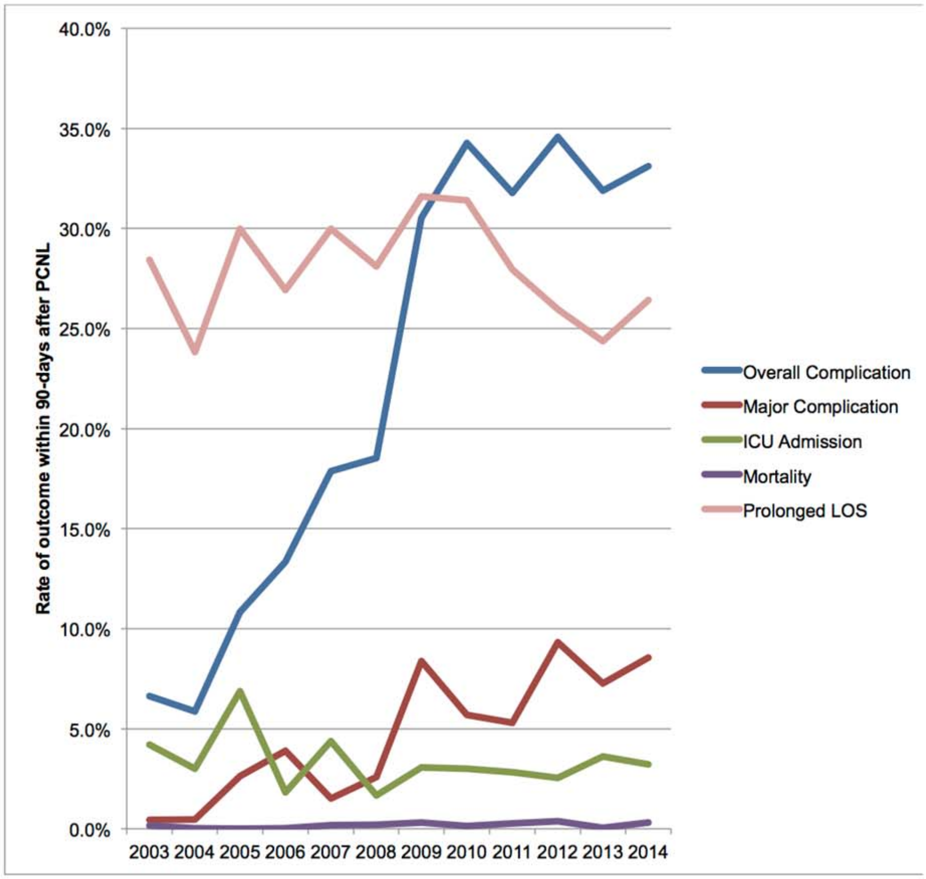

Figure 3. Trend Of 90-Day Postoperative Outcomes (Rates Of Overall Complication, Major Complication, ICU Admission, Mortality, Prolonged Length Of Stay) Among Patients Who Underwent PCNL From The Premier Healthcare Database In The United States From 2003 To 2014