Predictors of narcotic use after percutaneous nephrolithotomy

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Introduction: Percutaneous nephrolithotomy (PCNL) is associated with significant variability in postoperative pain and subsequent narcotic use. The purpose of this study was to determine the factors associated with high narcotic use following PCNL.

Materials and methods: A single-center retrospective review of patients undergoing initial PCNL between 2004 and 2014 was performed. Preoperative, intraoperative and postoperative factors associated with postoperative narcotic usage were analyzed. The primary outcome variable was mean narcotic usage, standardized to intravenous morphine-equivalents. Patients in the lowest 75th percentile were compared to those in the highest 25th percentile. Univariate and multivariate statistical analyses were performed, with p < 0.05 considered significant.

Results: When the 243 patients were compared from lowest to highest quartile, total narcotic use during the

Introduction

Percutaneous nephrolithotomy (PCNL) is the procedure of choice for most large renal calculi.¹ Although this procedure is a highly effective minimally invasive technique, it is still associated with significant postoperative morbidity and a significant variability in postoperative pain and subsequent narcotic usage. High levels of postoperative pain can lead to increased

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Address correspondence to Dr. D. Duane Baldwin, Department of Urology, Loma Linda University School of Medicine, 11234 Anderson Street, Room A560, Loma Linda, CA 92354 USA first 48 hour period was 2.3, 8.4, 15.6, and 41.7 mg of morphine-equivalents. On univariate analysis, predictors of high narcotic use included age 20-39 (p < 0.001), preoperative narcotic use (p < 0.001), presence of a postoperative complication (p = 0.044), and high stone burden (p = 0.002). Age < 20 (p < 0.001) and > 60 years (p = 0.014) were associated with low narcotic use. On multivariate analysis, age 20-39 (OR 6.87, 95% CI 2.22-21.23, p = 0.001), male gender (OR 2.47, CI 1.05-5.81, p = 0.037), and preoperative narcotic use (OR 3.27, CI 1.41-7.60, p = 0.006) were associated with higher opioid requirement.

Conclusion: Patients who were aged 20-39, males, and those with prior narcotic exposure used the highest doses of narcotics postoperatively. Knowledge of the factors predictive of high narcotic usage may allow better preoperative management of patient expectations and more effective postoperative care to prevent the complications of high narcotic usage.

Key Words: age, percutaneous nephrolithotomy, postoperative pain, narcotics, kidney stone

narcotic usage, prolonged hospital stay, chronic opiate dependence, and increased pulmonary and cardiovascular complications.²

Significant research has focused on reducing postoperative pain by technical modifications to the procedure including using smaller nephrostomy drainage tubes,³⁻⁶ tubeless PCNL,³ and mini-perc.⁷ However, no previous study has specifically reviewed preoperative patient characteristics to determine whether factors could be identified which would predict a patient's subsequent narcotic usage following PCNL.

The purpose of this study was to review a single institutional cohort, and systematically evaluate the preoperative, intraoperative, and postoperative factors that are associated with high narcotic use following initial PCNL.

Materials and methods

Following approval by the institutional review board (IRB), a retrospective review was performed of 269 patients undergoing initial PCNL between 2004 and 2014 at a single institution. Patients without in-hospital medication administration data were excluded from analysis (n = 26). Non-steroidal pain medications were not utilized in this population due to concerns for an increased bleeding risk.

All narcotic medications administered to the patient on postoperative day one and two were recorded. These narcotic medications were then converted to morphine-equivalents calculated using the GlobalRPH Advanced Opioid Converter.⁸

Specific preoperative factors studied included age, body mass index (BMI), gender, race, laterality, access location (upper, middle or lower pole), stone location, cross-sectional stone surface area, history of preoperative narcotic usage, preoperative urine culture, preoperative hemoglobin level, and preoperative creatinine level.

Intraoperative factors recorded included operative time, use of intraoperative flexible ureteroscopy, estimated blood loss (EBL), and transfusion rate.

Postoperative factors studied were complication rate, narcotic usage at 24 hours and 48 hours postoperatively, stone-free rate (SFR), change in hemoglobin level, and stone chemical composition.

The primary outcome variable was mean narcotic usage at 24 hours and 48 hours postoperatively, standardized to intravenous morphine-equivalents. In order to identify patients with high narcotic use, we compared patients in the 75th percentile to those in the 25th percentile. Univariate and multivariate statistical analyses were performed, with p < 0.05 considered significant.

Operative technique

PCNL cases were performed with the patient in the prone position. Conventional 34 Fr percutaneous renal tracts were utilized for all patients. Lithotripsy was performed using ultrasonic and laser lithotripsy combined with fragment extraction. All patients utilized the same nephrostomy tubes postoperatively which consisted of a 22 Fr Council tip catheter with a 5 Fr MPA reentry catheter (Cook, Bloomington, IN, USA) placed through the lumen of the Council tip catheter.

Results

There were 269 total initial PCNL procedures performed at a single academic institution. All procedures reviewed were initial PCNL procedures. Second look procedures were not utilized for data collection. Of these 269 procedures, 26 did not have complete pain medication data. This left a total of 243 patients with complete data sets for analysis.

The mean patient age was 49.2 years. Fifty-one percent of the patients were men and 49% were women. The mean narcotic use was 18.2 mg, in the first 24 hour postoperatively and 16.7 mg in the next 24 hours period.

The patients were divided into four quartiles based upon the equivalent amount of IV morphine administered postoperatively. The first three quartiles represented the group of patients who used the lowest amount of narcotics. The fourth quartile represented the group of patients who used the highest amount of narcotics. By quartile, mean narcotic usage during the first 48 hour post-operative period was 2.3, 8.4, 15.6, and 41.7 mg of morphine-equivalents, Table 1, Figure 1 and Figure 2. When the 182 patients in the lowest three quartiles of narcotic usage were compared to the 61 patients in the highest quartile of narcotic usage,





Characteristic	Low narcotic use bottom 75 th percentile	High narcotic use highest 25 th percentile	p value
Age (≤ 20)	15 (100.0%)	0 (0.0 %)	< .001
Age (20-39)	27 (49.1%)	28 (50.9%)	< .001
Age (40-59)	76 (75.3 %)	23 (24.7%)	0.623
Age (≥ 60)	64 (84.0%)	10 (16.0%)	0.014
Body mass index ≥ 30	77 (68.8%)	35 (31.3%)	0.165
Preoperative narcotic use	48 (59.3%)	33 (40.7%)	< .001
Postoperative complications	36 (63.2%)	21 (36.8%)	0.044
Thoracic complications	2 (50.0%)	2 (50.0%)	0.43
Overall stone burden	592.95 (610.51)	1137.32 (950.87)	0.002
Access location (upper)	82 (73.9%)	29 (26.1%)	0.848
Access location (mid/lower)	91 (72.8%)	34 (27.2%)	0.852
Access location (multiple)	5 (83.3%)	1 (16.7%)	0.61
Operative time	138.14 (60.43)	153.56 (85.71)	0.126
≥ 50% "hard stone"	98 (72.6%)	37 (27.4%)	0.703
(cystine, Ca Phos, Ca oxalate monohydrate)			
Gender (1 = male)	83 (69.2%)	37 (30.8%)	0.126
Race $(1 = white)$	125 (71.0%)	51 (29.0%)	0.273
Laterality $(1 = left)$	94 (74.0%)	33 (26.0%)	0.864
Preoperative urine culture, given appropriate preop antibiotics	83 (72.2%)	32 (27.8%)	0.776
Hb preop	13.23 (1.69)	12.87 (2.20)	0.217
Cr preop	1.07 (.67)	1.02 (.49)	0.603
At least 50% staghorn as described on op note	98 (72.6%)	37 (27.4%)	0.703
Ureteroscopy (antegrade or retrograde)	105 (80.2%)	26 (19.8%)	0.836
Stone-free after 1 st procedure	130 (74.3%)	45 (25.7%)	0.677
Transfusion rate	5 (55.6%)	4 (44.4%)	0.231
Estimated blood loss	122.62 (134.66)	135.70 (122.97)	0.497
Change in Hgb	-1.15 (1.10)	75 (1.60)	0.058

TABLE 1. Univariate analysis of preoperative and intraoperative factors affecting postoperative narcotic usage after 1st PCNL

there was no correlation between narcotic use and BMI (p = 0.165), operative time (p = 0.126), stone chemical analysis (p = 0.703), race (p = 0.273), laterality (p = 0.864), preoperative urine culture (p = 0.776), preoperative Hb (p = 0.217) and preoperative creatinine (p = 0.603). In addition, blood loss (p = 0.497) and access location (p = 0.848) were not associated with increased narcotic requirement.

The factors on univariate analysis that did predict high narcotic use during the first 24 hours and first 48 hours postoperatively included age 20-39 (p < 0.001), preoperative narcotic use (p < 0.001), presence of a postoperative complication (p = 0.044), and high overall stone burden (p = 0.002). Age < 20 (p < 0.001) and > 60 years (p = 0.014) were associated with low narcotic use.

On multivariate analysis, age 20-39 (OR 6.87, 95% CI 2.22-21.23, p = 0.001), male gender (OR 2.47, CI 1.05-5.81, p = 0.037), and preoperative narcotic use (OR 3.27, CI 1.41-7.60, p = 0.006) were associated with high narcotic use. No variables were associated with low narcotic use, Table 2 and Figure 3.

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Figure 2. Mean narcotic use per quartile over the first 48 hours postoperatively.



Figure 3. Multivariate analysis of statistically significant univariate factors

Discussion

Despite modifications in management of large staghorn calculi designed to reduce the invasiveness of their treatment, pain control following this procedure remains a significant disadvantage associated with this approach. Although PCNL is a minimally invasive technique followed by a rapid recovery, it still may be associated with a high level of pain perceived by the patient.3-5 In the present study, patients in the two upper quartiles of narcotic usage in the first 48 hours postoperatively used a total narcotic dose of 15.6 mg and 41.7 mg intravenous morphine equivalents, respectively. In comparison, a prior study of outcomes of standard laparoscopic versus hand-assisted laparoscopic donor nephrectomy found that the total analgesic use for the hospital stay was 22.1 mg and 28.3 mg of morphine equivalents, respectively.8 Similarly, a comparison of techniques for treating uretero-pelvic junction obstruction calculated 27.2 mg and 22.4 mg morphine equivalent dose of analgesia for the duration of the hospital stay for laparoscopic pyeloplasty and Acucise endopyelotomy, respectively.9 Xu and colleagues recently published the results of their enhanced

Factor	Beta-coefficient	Odds ratio	95% CI	p value
Age (20-39)	1.93	6.87	(2.22, 21.23)	0.001
Gender (male)	0.906	2.47	(1.05, 5.81)	0.037
Preoperative narcotic use	1.19	3.27	(1.41, 7.60)	0.006
Overall stone burden > 392 mm ²	0.857	2.36	(.86, 6.46)	0.096
At least 50% staghorn as described on op note	0.686	1.99	(.77, 5.14)	0.157
≥ 50% "hard stone"	0.722	2.06	(.83, 5.14)	0.121
(cystine, Ca Phos, Ca oxalate monohydrate)				

TABLE 2. Multivariate analysis

recovery protocol after radical cystectomy and found that adoption of the protocol decreased analgesic use from 20.67 mg of morphine equivalents per day to 4.9 mg.¹⁰ Furthermore, there is wide variation in the amount of pain medications used. Some patients will use little to no pain medication, while others will stay for several days, using high levels of opioid pain medications. This can lead to a vicious cycle, as opioid receptors may become oversaturated and no longer respond to opiate pain medications.² The observation that a seemingly minimally invasive surgery such as PCNL may at times result in such a high level of postoperative pain medication usage and also the observation that there is such a variation in the amount of pain medication used led us to hypothesize that there may be certain previously unreported factors specific to this surgery which can influence the amount of pain patients feel postoperatively.

Understanding the factors that increase patients' narcotic requirements in the postoperative period is important. Carroll et al² demonstrated that uncontrolled postoperative pain can lead to increased narcotic usage, chronic opiate dependence, increased pulmonary and cardiovascular complications, leading to morbidity and mortality in a cohort of patients chronically consuming opioids in the United States. However, there were no PCNL patients included in this series. To our knowledge, there has been no prior study focusing on the factors influencing postoperative pain medication usage specifically for PCNL patients. Multivariate analyses in this study have identified age (20-39), preoperative narcotic usage, and male gender as risk factors for high postoperative narcotic usage after PCNL.

Preoperative narcotic use, postoperative complication, and volume of stone burden were hypothesized to strongly influence post-operative narcotic usage. However, in age we did not anticipate significant differences in narcotic usage between different age groups. There is significant scientific literature attempting to study the effects of age on pain sensitivity to noxious stimuli and pain in the acute postoperative setting. Ledowski et al¹¹ assessing patients in the acute postoperative pain setting with subjective pain ratings as well as heart rate variability, heart rate, and blood pressure found no effect of age upon the amounts of pain. The patients in Ledowski's study were scheduled for minor elective general (e.g. hernia repair), plastic (e.g. hand surgery) and orthopaedic (e.g. osteosynthesis upper and lower limb) surgery and there were no PCNL patients in their study.

The effect of age upon pain threshold has been previously investigated. Lautenbacher et al found that somatosensory thresholds increased with age.¹²

This could be the reason that only middle age (20-39) was statistically significant for association with high narcotic usage on multivariate analysis.

The other factors associated with high postoperative narcotic usage that reached statistical significance on multivariate analysis were male gender and preoperative narcotic use. In our study, patients with preoperative opiate use required more than 3 times as much morphine for postoperative pain compared with opioid naïve patients. Carroll et al² and Angst et al¹³ reported that the increased postoperative narcotic usage was due to opioid-induced hyperalgesia (OIH). It is an alternative neuro-pharmacological phenomenon that may explain the need to escalate the opioid dose over time. Sometimes, administration of opioids may even induce an increased sensitivity to pain (hyperalgesia). The finding of preoperative narcotic use as a predictive factor for increased postoperative opioid has also been identified in studies of other sources of painful stimuli including in cancer patients undergoing surgeries, in patients undergoing gynecologic, orthopedic and general surgical procedures.^{14,15}

Our study is unique as it demonstrates for the first time that for patients undergoing a PCNL, the preoperative opioid user requires an increased opioid demand at an OR of 3.27. The presumed explanation for this finding lies in the development of tolerance to the opioid effects, in addition to opioid-induced hyperalgesia, thus pain relief requires higher dosing in order to effectively interact with the Mu receptors while increasing the risk for opiate side effects, like constipation, decreased ambulation, more deep venous thrombosis, more ileus, and more bloating.²

In our study, male gender had a statistically significant association with high narcotic usage on multivariate analysis. One possible explanation is that men have more muscles and thicker chest walls, and therefore could get more irritation with the nephrostomy tube with each respiration.

There has been considerable effort directed to evaluate multimodal pain management strategies and adjunct modalities for PCNL such as tubeless PCNL, mini-PCNL, local anesthetic infiltration of nephrostomy tract as well as renal capsule and intercostal nerves at time of surgery, and IV antiinflammatory continuous infusions.¹⁶⁻¹⁸ Our study may help to preoperatively identify those patients most likely to benefit from these modalities.

In 2013, Kirac et al¹⁷ concluded that the pain after tubeless and standard PCNL may be decreased by bupivacaine infiltration into the nephrostomy tract. Preminger et al¹⁶ noticed also a trend toward decreased postoperative narcotic use in patients receiving subcutaneous marcaine administration around the nephrostomy tube tract.

Infiltration with local anesthetic requires operative time and does pose a small but significant risk of complications such as pneumothorax or injury of the intercostal vessels. In 2013, Honey et al assessed 63 patients, and concluded that intercostal nerve blockade with bupivacaine significantly improves both pain control and health related quality of life in the early postoperative period.¹⁹

Multiple strategies were reported to reduce postoperative pain and opioid consumption following PCNL including NSAIDs, regional anesthesia (spinal or epidural) and IV paracetamol. However, it carries the risk of nephrotoxicity, theoretical increased bleeding risk, intraoperative hemodynamic instability technical difficulty and increased cost.²⁰⁻²⁷ These various adjunctive pain management strategies may be utilized, but inherently carry additional risk, resources, and time to implement.

In summary, it is crucial to be screening all surgical patients for any preoperative narcotic dependence, especially in young males, since it will affect postoperative outcomes. Adopting a strategy to minimize the use of opioids is of utmost importance, since an increase in postoperative pain is correlated with a decrease in a patient's quality of recovery in the immediate postoperative period.²⁸

Previous studies reported the predictors of postoperative pain and narcotic usage following URS and SWL. Gul et al reported that younger age, higher preoperative pain score, and stent placement were independent variables for higher postoperative pain and more narcotic use in the post-anesthesia care unit following URS.²⁹ Ahn et al reported that young age, psychiatric illness, history of urinary tract infection, use of a stone basket, large stone size, and prolonged operative time were predictors for postoperative pain.³⁰ For SWL, multiple studies have reported that young patient age, patients from Mediterranean countries, small aperture lithotripters and stones projecting over the rib were predictors for pain and higher analgesic usage.³¹

This study has some limitations. First, it was a retrospective study. Second, it did not directly measure pain, but assessed only the amount of narcotic required. Third, this study did not assess pain relief provided by mini-PCNL, tubeless PCNL, or nerve blocks. Finally, that we are a referral center with patients referred from outside facilities so the time from initial evaluation until referral cannot be captured. Long referral times could potentially lead to increased usage of narcotics. The purpose of this study was to understand preoperative factors associated with postoperative narcotic usage. As this was the goal in our study, perhaps future studies will be able to assess those factors in order to determine their effects on those mentioned surgical alternatives.

Conclusion

PCNL is a highly effective minimally invasive technique for the treatment of large upper urinary calculi, but it is accompanied by significant variability in postoperative pain and subsequent opioid use. Patients aged 20-39, males, and those with a prior prescription for narcotic pain medication require significantly higher doses of narcotics postoperatively for pain management. Early identification of these at risk patients may allow implementation of alternative strategies for pain control. In addition, knowledge of these risk factors for high narcotic requirements may allow strategies designed to reduce the effects of narcotic use.

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