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# The efficacy of bupivacaine infiltration along nephrostomy tract on postoperative pain control and opioid consumption after PCNL: a prospective randomized controlled trial

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**Abstract. – OBJECTIVE: Percutaneous nephrolithotomy (PCNL) is a common endourological procedure for patients with large kidney stones, but the management of postoperative pain is still a major challenge. The aim of this clinical trial was to evaluate the efficacy of 0.25% bupivacaine infiltration along the nephrostomy tract on postoperative pain scores and analgesia consumption in patients who underwent PCNL.**

**PATIENTS AND METHODS: A total of 50 patients who underwent PCNL were enrolled in this prospective, randomized controlled trial (NCT04160936). Patients were prospectively randomized into two equal groups: the study group (n=25) received 20 mL of 0.25% bupivacaine infiltration along the nephrostomy tract, whereas patients in the control group (n=25) did not. Postoperative pain as the primary outcome was assessed by using a visual analogue scale (VAS) and a dynamic visual analogue scale (DVAS) at different time points. The secondary outcomes were the time for first opioid demands, the number of opioid demands, and the total opioid consumption over the 48 h postoperatively.**

**RESULTS: There were no significant differences between the two groups regarding demographics, surgery, and stone characteristics. Patients in the study group had significantly less VAS and DVAS pain scores compared to the control group. The mean time of the first opioid demand in the study group was significantly longer as compared to the control group (7.1 ± 2.5h *vs.* 3.2 ± 1.8 h, $p<0.001$). The mean number of doses and total consumption of opioids were significantly less in the study group compared to the control group over 48 h (1.5 ± 0.8 *vs.* 2.9 ± 0.7 and 122.82 ± 62.5 mg *vs.* 223 ± 70 mg, respectively) ($p<0.0001$).**

**CONCLUSIONS: Local anesthetic infiltration of 0.25% bupivacaine along the nephrostomy tract is efficient in alleviating post-operative pain and reducing opioid consumption after PCNL.**

*Key Words:*
Percutaneous nephrolithotomy, Bupivacaine, Postoperative pain, Local anesthetic.

### Abbreviations

PCNL: Percutaneous nephrolithotomy, VAS: visual analogue scale, DVAS: dynamic visual analogue scale, LAI: local anesthetic infiltration, NSAIDs: non-steroidal anti-inflammatory drugs.

## Introduction

Worldwide, the incidence and prevalence of kidney stones have increased over the past decades with an estimated prevalence of around

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10% in the US alone[1]. There is also a dramatic increase in Europe and in the hot climate "stone belt" extending from the southeastern United States to northern Australia[2].

Percutaneous nephrolithotomy (PCNL) is a common minimally invasive procedure in urology practice and remains the standard surgical treatment for large renal stones with a high success rate, less morbidity, and short hospital stay in comparison to open surgery[3,4]. Nevertheless, post-operative pain following PCNL is a major clinical challenge, caused by the distention of the renal capsule and parenchyma[5,6]. Moreover, the movement of the access (Amplatz) sheath is associated with considerable pain because of the irritation in the diaphragm, pleura, and retroperitoneum. Furthermore, stretching of the skin, subcutaneous fat, muscles, and the presence of a nephrostomy tube may contribute to the pain after PCNL[7].

Currently, there is no standard approach for postoperative pain management after PCNL. Various options include the use of systemic opioids, non-steroidal anti-inflammatory drugs (NSAIDs), patient-controlled analgesia pumps, epidural analgesics, and local anesthetic infiltration (LAI)[8,9]. In clinical practice, there are established roles of NSAIDs and opioids in pain control, but still, there are major concerns of adverse events which limit their use, particularly in high-risk patients, such as the elderly or those with preexisting renal insufficiency.

Treatment with NSAIDs and opioids may be associated with serious gastrointestinal, renal, and cardiovascular problems, respiratory depression, sedation, and other side effects[10-12]. Therefore, LAI prevents patients from such serious morbidities by reducing the use of NSAIDs and opioids[13].

Hence, appropriate, and adequate treatment of pain following PCNL reduces the rate of morbidities, hospital stays, and costs. Recently, several studies[9,14-18] describing the efficacy of LAI in pain control after PCNL presented favorable outcomes, with considerable methodological differences existing in terms of blinding, the timing of the block, and the type of anesthetic agents. Wang et al[19], in a meta-analysis, concluded that there were no significant differences between groups in terms of hospital stay, duration of the procedure, and hemoglobin level. On the other hand, they showed that patients in the study group had less consumption of analgesia, the time of first analgesic demand, and less post-operative pain score compared to patients in the control group.

At present, there are no clear recommendations concerning the optimal approach for pain management following PCNL, and the role of routine LAI in the nephrostomy tract is still controversial. We conducted this study to investigate the efficacy of 0.25% bupivacaine infiltration along the nephrostomy tract on postoperative pain control and opioid consumption in patients undergoing PCNL.

## Patients and Methods

### Study Design and Approval

This is a prospective, randomized, double-blind, controlled, multicenter study conducted between February 2018 and September 2020. The ethical approval was obtained by the Institutional Review Board at Jordan University Hospital (IRB #10/2017/358) and registered on clinicalTrials.gov (NCT04160936). Before attaining written informed consent, the study design, procedures, and outcomes measuring instruments were explained to patients in accordance with the Declaration of Helsinki.

### Inclusion and Exclusion Criteria

Patients who were 18 to 70 years old, with kidney stone size >2 cm and body mass index (BMI) <35 were included in the study. Patients with excessive intraoperative bleeding, kidney stones requiring more than a single puncture, allergy to local anesthetics, active urinary tract infection, surgical procedure extending more than 3 hours, drug allergies, bilateral simultaneous PCNL, severe cardiopulmonary disease, abnormal renal function tests, psychiatric diseases, bleeding disorders, and refusal to participate, were excluded from the study.

### Patient Recruitment and Randomization

Fifty patients with large kidney stones who were scheduled for PCNL were invited to participate in the study. Patients were randomized into two groups using a computer-generated randomization scheme. The study group included patients who received nephrostomy tract infiltration with 20 ml of 0.25% bupivacaine, and the control group included patients who did not receive it. The study participants and the post-operative independent observer were blinded.

### Technique

All procedures were performed under general anesthesia by senior urology surgeons experienced in endourology and percutaneous renal surgery in two different hospitals. At the time of anesthesia induction, all patients received intravenous antibiotics and remained at the hospital. Then they were discharged and took oral antibiotics for another 3 days. An open-end 6 Fr ureteral catheter was inserted by cystoscope (Storz, Germany) into the ureter in the lithotomy position and the urinary bladder was drained with a 16 F indwelling urethral catheter. Under fluoroscopic guidance in the prone position, contrast media was injected *via* the ureteral catheter. Renal access was created by the biplane technique of standard PCNL. After the tip of the needle was in the collecting system, sensor tip guide wire was inserted followed by tract dilatation using Amplatz and balloon dilators (Boston Scientific, USA) up to 30 F. Stone was disintegrated with ultrasonic and/or pneumatic lithotripsy and retrieved through rigid 26 Fr nephoscope (Storz, Germany). At the end of the procedure nephrostomy tube (size 16 F) was routinely inserted in all cases. The nephrostomy tube was removed on the first or second postoperative day unless a complication occurred and required an extended period of drainage. A successful procedure was defined as stone-free or residual fragments smaller than 4 mm assessed with plain radiography or abdominal CT scan.

After insertion of the nephrostomy tube and before the extubation, in patients of the study group, a 23-gauge, 90 mm spinal needle was inserted up to the renal capsule under fluoroscopic guidance along the nephrostomy tube at 6 and 12 o'clock position; then 0.25% bupivacaine was infiltrated into the nephrostomy tract, while gradually withdrawing the needle from renal capsule to the skin thereby infiltrating the renal capsule, perinephric fat, muscles, subcutaneous tissue, and skin (Figures 1 and 2). Patients in the control group did not receive any infiltration.

### Patient Assessment and Outcomes

On admission to the hospital, all patients were evaluated preoperatively by medical history, physical examination, basic laboratory tests, and radiological investigations including abdominal CT scan.

Postoperatively, a VAS score (0-10) was used for the evaluation of pain at rest and a DVAS score (0-10) was used during coughing and deep breathing with 0 being no pain and 10 being maximum, unbearable pain. VAS and DVAS scores were obtained by an independent observer who was blinded to the randomization order at 1, 4, 8, 12, 24, and 48 hours post-operatively. Intramuscular pethidine 1 mg/kg was given when VAS or DVAS scores were ≥4, as a rescue analgesic, and the patient was reassessed. A maximum of 500 mg of pethidine was given in the first 24 hours.

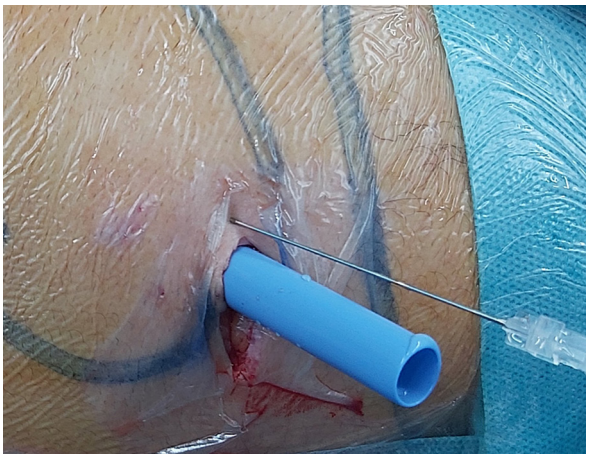

**Figure 1.** Bupivacaine infiltration near the nephrostomy tract.

The primary outcome of this study was to evaluate postoperative pain as measured by the VAS and DVAS scores at various time points. The time

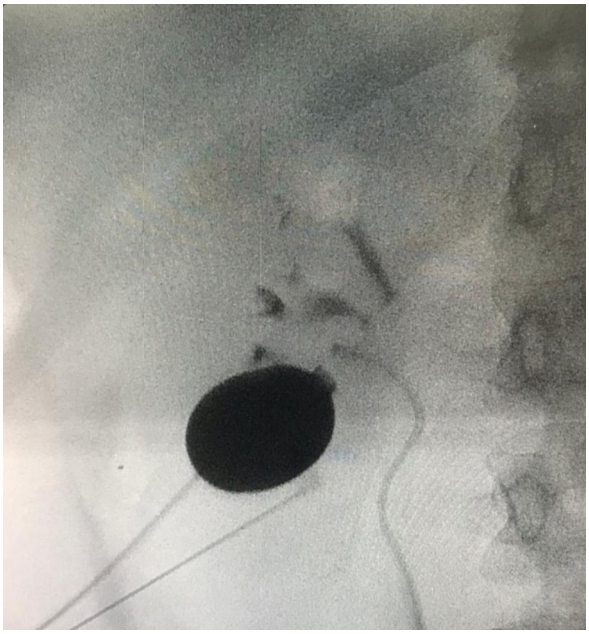

**Figure 2.** Intraoperative fluoroscopic view of peritubal injection.

for the first opioid demand, the number of opioid demands, and the total opioid intake were recorded as secondary outcomes. In addition, operative time, blood transfusion, residual stones, length of hospital stay, serum creatinine, hemoglobin, and hematocrit in the perioperative period were measured.

### *Statistical Analysis*

Continuous variables were depicted as mean± standard deviation (SD) or median and interquartile range (IQR) based on data distribution. Categorical variables were described as numbers and percentages. Clinical characteristics and outcomes were compared between patients who received local anesthetic infiltration using the *t*-test or Wilcoxon rank test for continuous variables and the Chi-square test or Fisher's exact test for categorical variables. All tests were two-sided, and statistical significance was set at *p*-value ≤0.05. The analysis was carried out using SPSS version 22 (IBM Corp., Armonk, NY, USA).

The sample size was calculated based on power analysis using α of 5% and β of 20%. A minimum of 44 patients (22 per group) was determined to show a 15% difference in pain scores.

## Results

Figure 3 summarizes patients' enrollment process, allocation, follow-up, and final analysis in both groups. In the study group, 25 patients were included in the final analysis and 25 patients were in the control group.

There were no significant differences between groups with regard to age, gender, BMI, stone burden, laterality, extra-corporeal shock wave lithotripsy (ESWL) sessions, and tract length. Also, there were no significant differences observed among the groups in terms of mean operative time, blood loss, blood transfusion, postoperative complications, residual stones, length of hospital stay, serum creatinine, and hematocrit in the

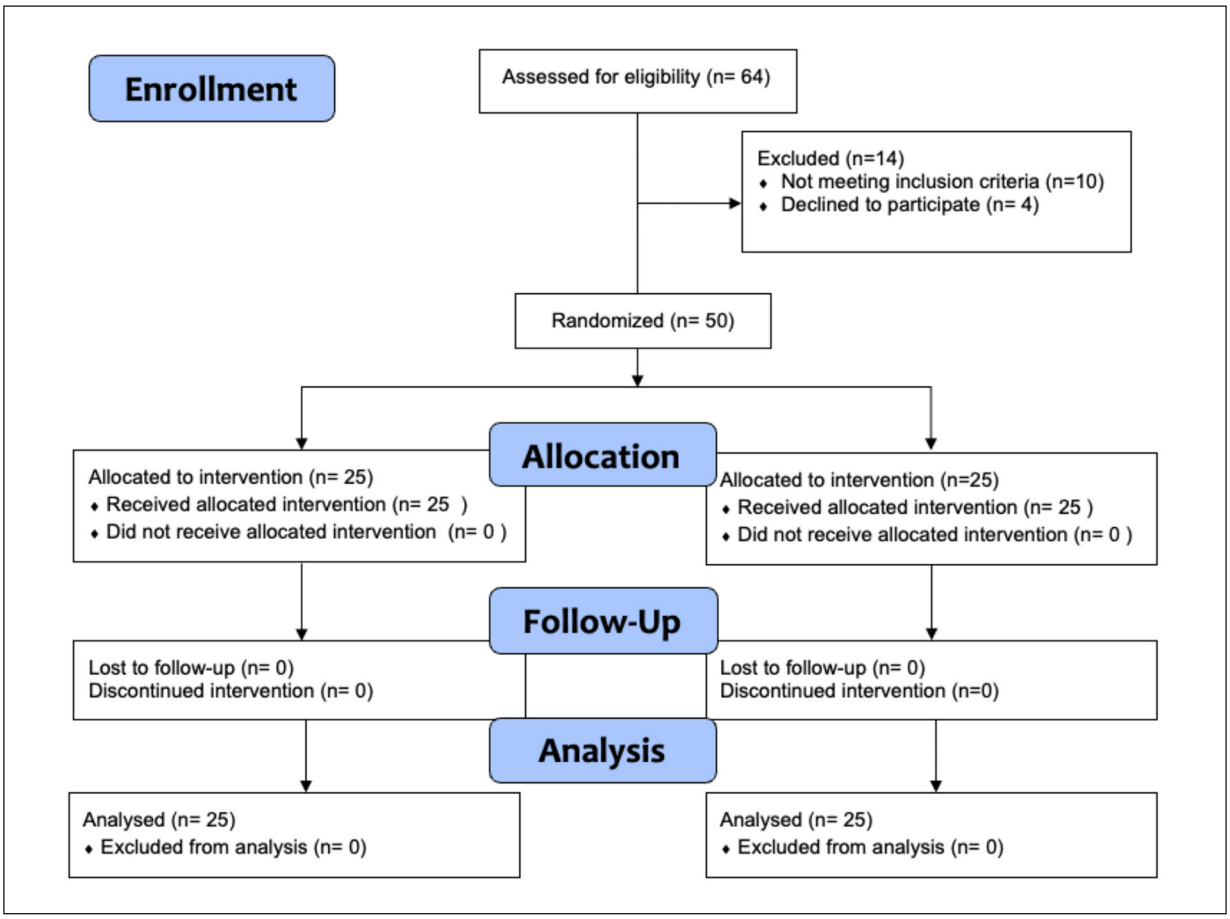


**Figure 3.** Flow of patients during the study period.

perioperative period. Post-operative hemoglobin level was significantly lower in the control group ($p$=0.038). Comparison of postoperative complications in terms of the Modified Clavien Classification between the groups did not indicate any significant difference ($p$=0.7) (Table I).

Figure 4 shows the VAS at rest, while Figure 5 shows DVAS during coughing and deep breathing. When post-operative pain, as a primary outcome, was analyzed in both groups using VAS and DVAS at 1, 4, 8, 12, 24, and 48 hours, mean VAS was significantly lower in the study group at 1, 4, 8 hours compared to the control group: 1.7±1.12 *vs.* 4±1.5, 2.5±1.5 *vs.* 5.7±1.6, 5.1±1.4 *vs.* 6.9±1.4, respectively. While mean DVAS was significantly lower in the study group at 1, 4, 8, 12 hours compared to the control group: 2.2±1.3 *vs.* 5.2±1.5, 2.8±1.8 *vs.* 6.6±1.5, 5.1±1.9 *vs.* 7.8±1.2, 3.4±1.7 *vs.* 5±1.5 respectively. VAS and DVAS were comparable at and after 12 and 24 hours, respectively (Table II).

Postoperative opioid consumption was recorded over 48 h. The mean time for first opioid demands was significantly longer in the study group compared to the control group (7.1±2.5 h *vs.* 3.2±1.8 h, $p$<0.001). Also, the mean number of opioid demands was significantly lower in the study group 1.5±0.8 compared to the control group 2.9±0.7, ($p$<0.001). The mean total opioid consumption was significantly lower in the study group 122.82±62.5 mg as compared with 223±70 mg in the control group, ($p$<0.0001) (Table III).

## Discussion

PCNL remains the standard procedure for large renal stones, with high success rates, and less invasiveness compared to open surgery[3,4,20]. Despite being a minimally invasive intervention, PCNL still causes significant post-operative pain, particularly in standard PCNL with a nephrostomy tube. Pain affects the postoperative quality of life, especially in the recovery period with the patient's anxiety and several negative aspects such as delayed mobilization, increased postoperative complications, and pro-

**Table I.** Baseline demographic and clinical characteristics in study and control groups.

| Variables | Study group (n = 25) | Control group (n = 25) | p-value |
|---|---|---|---|
| Age (years) mean ± SD | 45.8 ± 10 | 51.5 ± 10.3 | 0.05 |
| Gender | | | 0.2 |
| Male (n) | 17 | 12 | |
| Female (n) | 8 | 13 | |
| BMI (kg/m$^2$) mean ± SD | 26.7 ± 3.7 | 28.7 ± 5.4 | 0.1 |
| Stone burden (mm$^2$) mean ± SD | 25.3 ± 7 | 26.4 ± 10.2 | 0.1 |
| Laterality | | | |
| Right (n) | 10 | 13 | 0.4 |
| Left (n) | 15 | 12 | |
| ESWL sessions | | | 0.3 |
| No (n) | 18 | 21 | |
| Yes (n) | 7 | 4 | |
| Tract length (mm) mean ± SD | 101.7 ± 19 | 112.3 ± 20 | 0.3 |
| Operative time (min) mean ± SD | 71.1 ± 20.2 | 83.7 ± 26.5 | 0.07 |
| Blood loss (ml) median (range) | 50 (50-100) | 50 (40-100) | 0.5 |
| Blood transfusion (n) | 2 | 1 | 0.9 |
| Residual stones (n) | 2 | 2 | - |
| Complication (n) | | | 0.7 |
| Grade I | 20 | 21 | |
| Grade II | 5 | 4 | |
| Hospital stays (days) mean ± SD | 2.6 ± 0.6 | 3 ± 1.3 | 0.6 |
| Preoperative Creatinine (mg/dl) mean ± SD | 0.8 ± 0.2 | 0.9 ± 0.5 | 0.2 |
| Postoperative Creatinine (mg/dl) mean ± SD | 0.8 ± 0.2 | 0.9 ± 0.5 | 0.2 |
| Preoperative HTC mean ± SD | 43.3 ± 4.7 | 41 ± 6.2 | 0.1 |
| Postoperative HTC mean ± SD | 39.9 ± 5.9 | 37.3 ± 6.5 | 0.1 |
| Preoperative Hb (g/dl) mean ± SD | 14.2 ± 1.8 | 13.5 ± 2.2 | 0.2 |
| Postoperative Hb (g/dl) mean ± SD | 13.3 ± 1.8 | 12.1 ± 2.1 | **0.038** |

SD: standard deviation; BMI: Body Mass Index; ESWL: Extra-corporeal Shock Wave Lithotripsy; Hb: Hemoglobin; HTC: Hematocrit.

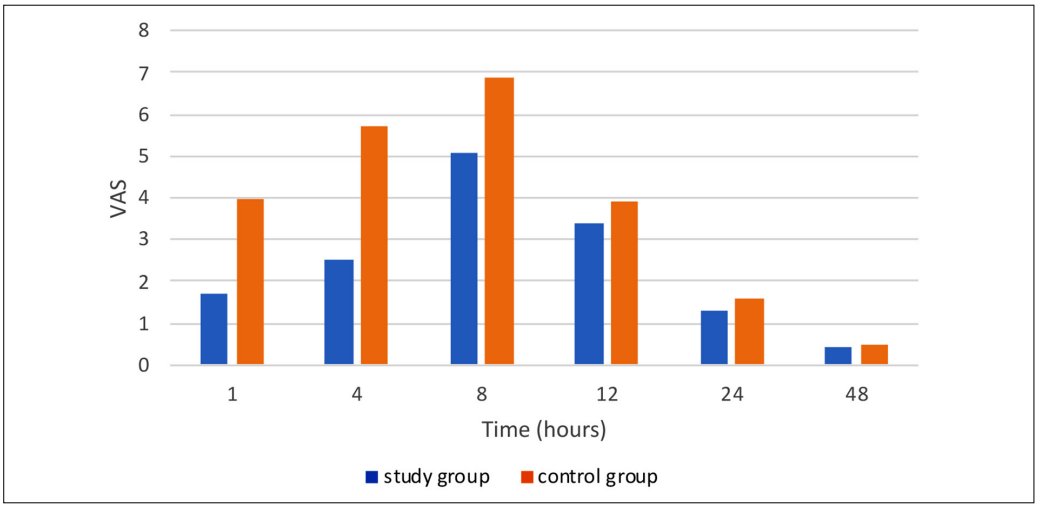


**Figure 4.** Mean visual analog scale.

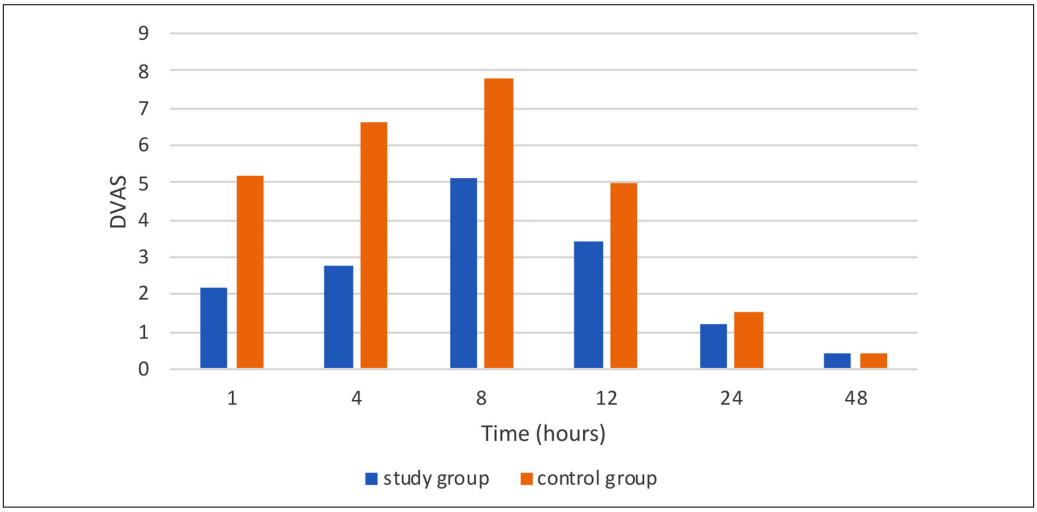


**Figure 5.** Mean dynamic visual analog scale.

**Table II.** Baseline demographic and clinical characteristics in study and control groups.

| Variables | Study group (n = 25) mean ± SD | Control group (n = 25) mean ± SD | *p*-value |
|---|---|---|---|
| VAS1 | 1.7 ± 1.12 | 4 ± 1.5 | < 0.001 |
| VAS4 | 2.5 ± 1.5 | 5.7 ± 1.6 | < 0.001 |
| VAS8 | 5.1 ± 1.4 | 6.9 ± 1.4 | < 0.001 |
| VAS12 | 3.4 ± 1.2 | 3.9 ± 1.1 | 0.1 |
| VAS24 | 1.3 ± 0.8 | 1.6 ± 1 | 0.2 |
| VAS48 | 0.4 ± 0.33 | 0.48 ± 0.4 | 0.6 |
| DVAS1 | 2.2 ± 1.3 | 5.2 ± 1.5 | < 0.001 |
| DVAS4 | 2.8 ± 1.8 | 6.6 ± 1.5 | < 0.001 |
| DVAS8 | 5.1 ± 1.9 | 7.8 ± 1.2 | < 0.001 |
| DVAS12 | 3.4 ± 1.7 | 5 ± 1.5 | 0.002 |
| DVAS24 | 1.2 ± 0.8 | 1.5 ± 1.1 | 0.3 |
| DVAS48 | 0.44 ± 0.4 | 0.44 ± 0.4 | 0.9 |

SD: Standard deviation; VAS: Visual Analog Scale; DVAS: Dynamic Visual Analog Scale.

**Table III.** Comparison of analgesic outcomes between the study and control groups.

| Variables | Study group (n = 25) | Control group (n = 25) | *p*-value |
|---|---|---|---|
| Time to first opioid demands (hours) mean ± SD | 7.1 ± 2.5 | 3.2 ± 1.8 | < 0.001 |
| No. of opioid demands mean ± SD | 1.5 ± 0.8 | 2.9 ± 0.7 | < 0.001 |
| Total consumption of opioids (mg) mean ± SD | 122.82 ± 62.5 | 223 ± 70 | < 0.001 |

SD: Standard deviation.

longed hospitalization[21-23]. Currently, there is insufficient evidence on the optimal approach for postoperative pain management after PCNL. In this study, we assessed the efficacy of 0.25% bupivacaine infiltration along the nephrostomy tract on postoperative pain scores and analgesia consumption after PCNL. Results from this study are consistent with previous studies[14-18], and we showed that 0.25% bupivacaine local infiltrations provided less postoperative pain score and reduced opioid consumption in comparison to the control group.

While narcotic analgesics are one of the main options for postoperative pain treatment, their use is limited after major surgical interventions due to their adverse effects. Thus, narcotic analgesics that are accepted as a standard option in the treatment of acute postoperative pain are now being replaced by the method of multimodal analgesia. A synergic effect is obtained using different drugs that influence the central and peripheral nervous systems. Additionally, fewer side effects may be achieved in comparison to analgesia using a single agent[24].

Several reports[9,14-18] are available on the efficacy of LAI for pain management following PCNL. Most of these studies[9,14-18] reported a significant reduction of postoperative pain when local anesthetic agents were infiltrated along the nephrostomy tract. Nevertheless, the interpretation of the outcomes from these previous studies[9,14-18] is difficult and challenging. In these studies[9,14-18], the type of local anesthetic agents, randomization groups, different periods of pain assessment, the recommended drug concentrations, and the techniques of drug administration along the nephrostomy tract varied widely.

Our results are consistent with several earlier investigations[14,15]. Parikh et al[14] evaluated sixty patients randomized to receive 0.25% bupivacaine or normal saline along the nephrostomy tract. The authors reported that DVAS, total requirement of tramadol, rescue analgesic requirements, and the first request for analgesia were significantly lower in the study group than those in the control group. Also, Lojanapiwat et al[15], reported that patients in the study group had significantly lower pain scores and less opioid consumption. In our study, we used pethidine as a rescue analgesic instead of tramadol, and the overall follow-up time was 48 h. We found that both pain scores and total consumption of pethidine were significantly lower among patients in the study group as compared to patients in the control group.

Furthermore, different types, techniques of administration, and concentrations of local anesthetics have been used in the management of post-PCNL pain. Dundar et al[9] compared three groups of patients with different doses of 0.5%, 0.25% bupivacaine, and a control group. Pain scores were recorded at different time points over 48 hours and significant differences were found only in the values measured in the 2nd hour, and no significant difference was found in values measured at other times. Also, the authors[9] found that there was no difference between the groups in terms of the total amount of analgesic usage. The first analgesic administration in the group that received 0.5% bupivacaine was significantly later than the group that received 0.25% bupivacaine 86±98 *vs.* 44±21 min.

The paravertebral block is another method of pain management after PCNL. Several studies[17,25,26] have been conducted with variable methodologies and results. Baldea et al[25] reported that patients in the paravertebral block group had significantly lower intraoperative opioid use, postoperative opioid use, frequency of opioid use, lower postoperative VAS pain scores, and antiemetic. Similarly, Yayik et al[17] investigated the efficacy of peritubal infiltration of 0.25 % bupivacaine and ultrasound-guided low thoracal paravertebral block in patients after PCNL. Patients in the paravertebral block group reported less VAS, and fentanyl consumption compared to the control and nephrostomy tract infiltration groups.

Soni et al[26] randomized 60 patients into two groups and they compared the efficacy of ropivacaine with fentanyl or dexmedetomidine when infiltrating the nephrostomy tract. The authors[26] conclude that the addition of dexmedetomidine to ropivacaine was found to be more effective than fentanyl in terms of prolongation of analgesic efficacy of local anesthetic in nephrostomy tract block along with short-lived mild sedation.

Parikh et al[18] evaluated 100 adult patients who underwent PCNL and were randomized to the bupivacaine group and ropivacaine group. VSA and DVAS at 6 h and 8 h in the bupivacaine group were significantly higher than in the ropivacaine group. The mean time to first rescue analgesia in the ropivacaine group was significantly longer than in the bupivacaine group. The mean number of doses of tramadol and total consumption of tramadol in 24 h was lower in the ropivacaine group though not statistically significant.

### Limitations

There were several limitations to this study. First, the sample size of the studies included was relatively small. Second, we excluded patients with more than one puncture, therefore we were unable to assess the efficacy of LAI on patients with more than one puncture. Moreover, other long-acting agents with different doses would be likely to provide further benefit and should be evaluated in future studies. The effect of different operators could not be accounted for in our analysis, and this might be a factor in postoperative outcomes. Despite this limitation, the study design and balanced groups can give a clear answer to our research question.

## Conclusions

Our results revealed that 0.25% bupivacaine local infiltration is efficient in postoperative pain control as patients in the study group had significantly lower pain scores compared to the control group. Furthermore, there was less need for opioid consumption as indicated by a decrease in the number of opioid demands, total opioid consumption, and significantly longer time for first opioid demands compared to the control group.

### Conflict of Interest

The Authors declare that they have no conflict of interests.

### Acknowledgements

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### Ethics Approval

This study was conducted according to the Declaration of Helsinki principles. The ethical approval was obtained by The Institutional Review Board at Jordan university hospital (IRB #10/2017/358).

### Availability of Data and Materials

The data that support the findings of this study are not publicly available due to privacy or ethical restrictions but are available from the corresponding author on reasonable request.

### Funding

The authors have no funding to report.

### Informed Consent

Written informed consent form was provided from all patients.

### Authors' Contribution

All authors had full access to all the data in the study and take responsibility for the integrity of the data and accuracy of the data analysis. Saddam H. Al Demour: manuscript writing/editing, data collection, conceived and designed the analysis, main conceptual idea, and design of the research. Omar M. Halalsheh, Rami S. Al-azab, Mohammad T. Al-Zubi, Samer F. Al-Rawashdah: research design, performance of the research, data collection, drafting of the manuscript. Marwan Ibrahim, Ahmad K. Abubaker, Abdelkarim S. Aloweidi, Mahmoud M. Almustafa: data analysis, drafting of the manuscript and data collection.

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