

## นิพนธ์ต้นฉบับ

### ผลของการบรรเทาความเจ็บปวดของผู้ป่วยที่ได้รับยาบิวพิวาเคน ในช่องท้องบริเวณตำแหน่งไตเดิมหลังได้รับการผ่าตัด เพื่อบริจาคไตโดยการส่องกล้อง

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#### บทคัดย่อ

**วัตถุประสงค์:** เพื่อศึกษาประสิทธิภาพของยาบิวพิวาเคนที่หยอดบริเวณไตเดิม ในการบรรเทาอาการปวดและลดปริมาณยาแก้ปวดที่ผู้ป่วยได้รับ ภายหลังจากการผ่าตัดเพื่อบริจาคไตโดยการส่องกล้อง

**ผู้ป่วยและวิธีการศึกษา:** ผู้ป่วยที่เข้ารับการผ่าตัดบริจาคไตโดยการส่องกล้องในโรงพยาบาลศิริราช ระหว่างเดือนมีนาคม ถึงสิงหาคม 2556 จำนวน 20 คน โดยผู้ป่วยแต่ละคนจะได้รับการหยอดยาปริมาณ 20 มิลลิลิตร บริเวณตำแหน่งไตเดิม ภายหลังจากการผ่าตัด ซึ่งได้รับการสุ่มแบ่งเป็น 2 กลุ่ม คือ กลุ่มที่ได้รับยาบิวพิวาเคน และกลุ่มที่ได้รับน้ำเกลือ ผู้ป่วยจะได้รับการประเมินความปวดโดยมาตรวัดความปวดแบบตัวเลข และได้รับยาแก้ปวดตามระดับความปวด ผลการศึกษาจะถูกนำมาเปรียบเทียบในแต่ละกลุ่มและคำนวณทางสถิติ

**ผลการศึกษา:** ภายหลังจากการผ่าตัด 12 ชั่วโมง กลุ่มผู้ป่วยที่ได้รับการหยอดน้ำเกลือ ต้องการค่าเฉลี่ยปริมาณยาแก้ปวดมอร์ฟีนมากกว่ากลุ่มผู้ป่วยที่ได้รับการหยอดยาบิวพิวาเคน (3 มิลลิกรัมและ 1.5 มิลลิกรัม ตามลำดับ) แต่ไม่มีความแตกต่างกันทางสถิติ ( $p=0.912$ ) นอกจากนี้ ผู้ป่วยในกลุ่มที่ได้ยาบิวพิวาเคน มีคะแนนปวดในขณะที่ปวดครั้งแรก และเมื่อได้รับยาแก้ปวดครั้งแรกน้อยกว่าในกลุ่มที่ได้รับน้ำเกลือ (คะแนน 4 และ 5 ตามลำดับ) โดยระยะเวลาที่ผู้ป่วยรู้สึกปวดและต้องการยาแก้ปวดภายหลังจากการผ่าตัดในกลุ่มที่ได้รับการหยอดยาบิวพิวาเคนยาวนานกว่าในกลุ่มที่ได้รับการหยอดน้ำเกลือ อย่างไรก็ตามไม่มีนัยสำคัญทางสถิติ

**สรุป:** ผู้ป่วยหลังได้รับยาบิวพิวาเคนบริเวณตำแหน่งไตเดิมภายหลังจากการผ่าตัดเพื่อบริจาคไตโดยการส่องกล้อง มีแนวโน้มที่จะได้รับยาแก้ปวดลดลงในช่วงแรกภายหลังจากการผ่าตัด นอกจากนี้ ยังมีการลดลงของคะแนนปวดและมีอาการปวดช้ากว่า อย่างไรก็ตามการศึกษานี้เป็นการศึกษานำร่อง จึงต้องมีการศึกษาเพิ่มเติมต่อไป

**คำสำคัญ:** บิวพิวาเคน, ผ่าตัดบริจาคไตโดยการส่องกล้อง, ความปวดหลังผ่าตัด

**กิตติกรรมประกาศ** โครงการวิจัยได้รับทุนอุดหนุนการวิจัยจากคณะแพทยศาสตร์ศิริราชพยาบาล มหาวิทยาลัยมหิดล รหัสโครงการ (IO) R015631017

## Original article

## The Reduction of Postoperative Pain in Laparoscopic Live Donor Nephrectomy after Bupivacaine Instillation at Renal Bed

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### Abstract

**Objective:** To evaluate the efficacy of bupivacaine instillation at the renal bed in reduction of postoperative pain and analgesic drugs.

**Material and Methods:** Twenty patients who underwent laparoscopic live donor nephrectomy from March 2013 to August 2013 at Siriraj Hospital were randomly divided into two groups, the normal saline and bupivacaine groups. At the end of the operation, an agent was introduced at the renal bed. Each patient was given 20 ml of normal saline or 0.5% bupivacaine, according to the group. The numeric rating scale was used to assess the patients' pain score. The patients were given the analgesic drugs according to their pain scores. Data were compared between the groups and statistically analyzed.

**Results:** There was no difference in the characteristics between the groups. The patients in the normal saline group required more total morphine at postoperative 12 hours (3 mg VS 1.5 mg), but this finding failed to reach statistical significance ( $p=0.912$ ). In the bupivacaine group, the median pain score at first pain was lower than in the normal saline group (4 VS 5;  $p=0.796$ ). In addition, the median pain scores of the patients in bupivacaine group at the time of the first required analgesic drug were lower, as well (4 VS 5;  $p=0.579$ ). Time to first pain and to the first analgesic requirement was longer in the bupivacaine group; however, there was no significant difference (165 VS 70 minutes;  $p=0.529$  and 235.5 VS 117 minutes;  $p=0.796$ ). There was no major complication in this study.

**Conclusion:** Bupivacaine instillation at the renal bed in the patients undergoing laparoscopic live donor nephrectomy trends to reduce analgesic usage in the early postoperative period. The pain scores at first pain were lower in the bupivacaine group. In addition, time to first pain and the first analgesic requirement were longer in the bupivacaine group. This was a pilot study, thus the sample size was limited.

**Keywords:** bupivacaine, laparoscopic donor nephrectomy, postoperative pain

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## Introduction

In Thailand, the number of patients with end stage renal disease has been increasing at about 0.15% of the Thai population.<sup>(1)</sup> They need renal replacement therapy, such as dialysis or renal transplantation. As a result, renal transplantation (deceased or living donor) has become a standard treatment for the patients who can afford it.

Eight hundred kidney transplantations have been performed at Siriraj Hospital in the past 37 years. Live donor nephrectomy has increased to about 41% of all kidney transplantations.<sup>(2)</sup> Laparoscopic nephrectomy becomes more favorable than an open surgical approach because of its significant health care benefits, such as shorter hospital stay, less blood loss, and a decrease in postoperative analgesia.<sup>(3,4)</sup> However, many patients still experience significant pain that requires analgesic drugs, including opiates, during their early recovery period. The exact etiology of post laparoscopic pain remains unclear. It appears to be multifactorial, such as port-site incision and peritoneal distension. There are different studies about local anesthetic drugs at surgical sites after laparoscopy in gynaecologic and intraabdominal surgery that decreased postoperative pain and thus the need for analgesic drugs.<sup>(5-14)</sup> To the best of our knowledge, this method has not been reported in laparoscopic nephrectomy. This study was designed to investigate the efficacy of local anesthetic drugs in the reduction of postoperative pain and analgesic drugs by the instillation of bupivacaine at the renal bed after laparoscopic live donor nephrectomy.

## Material and Methods

This prospective, randomized, controlled

clinical trial was approved by the Ethics Committee at Siriraj Institutional Review Board. Twenty patients who underwent laparoscopic live donor nephrectomy from March 2013 to August 2013 at Siriraj Hospital were recruited into the study. Informed consent was obtained from all patients.

The patients were randomly divided into two groups, the normal saline and bupivacaine groups. The operations were performed via a transperitoneal approach with 3 ports (as Figure 1 shows). The kidney was retrieved via a 7-9 cm Pfannenstiel incision which offered at the cosmetic benefit. Only fentanyl was given for analgesia during the perioperative period. At the end of the operation, after the kidney was removed and bleeding was checked and stopped, an agent was introduced at the renal bed (as Figure 2 shows). The patients were given 20 milliliters of the agent, normal saline or 0.5% bupivacaine, according to the randomization. Twenty milliliters of 0.25% bupivacaine were injected into the port-site incision of all participant patients. No drain was placed. Postoperative pain scores were evaluated at 1, 2, 3, 4, 6, 8, 12, 24 and 72 hours. During the postoperative period, the patients were prescribed 2 tablets of 500 milligrams of acetaminophen if their pain score was 4-6, and 0.05-0.1 milligrams per kilogram of intravenous morphine if their pain score was 7-10. The Numeric Rating Scale (NRS) was used to assess the patients' pain. Statistical analysis was conducted using Student's t test and Mann-Whitney test. A p-value < 0.05 was considered statistically significant.

## Results

Twenty patients were entered into the study and randomized into the normal saline and bupivacaine groups. The characteristics of the

patients including sex, age, BMI, operative time and the amount of intraoperative fentanyl, are shown in Table 1. There was no difference in the characteristics between the groups.

In the bupivacaine group, the median pain score at first pain was lower than in the normal saline group (4 VS 5;  $p=0.796$ ). In addition, the median pain scores of the patients in the bupivacaine group at the time of the first required analgesic drugs were lower, as well (4 VS 5;  $p=0.579$ , Table 2).

Mean time to first pain and to the first required analgesic drugs in the bupivacaine group were also longer than in the normal saline group.

However, there was no significant difference (165 VS 70 minutes;  $p=0.529$  and 235.5 VS 117 minutes;  $p=0.796$ ).

The patients in both groups required the same total amount of analgesic usage at postoperative 6 and 8 hours (1 gram acetaminophen and 1.5 mg morphine, Figure 3 and 4). However, the patients in the normal saline group required more total parenteral morphine at postoperative 12 hours (3 mg VS 1.5 mg;  $p=0.912$ ), as shown in Figure 4. Conversely, the patients in the bupivacaine group required more total oral acetaminophen at postoperative 12 hours (1.5 g VS 1.0 g;  $p=0.971$ ).

**Table 1.** Characteristics of the patients

	Normal saline Mean $\pm$ SD	Bupivacaine Mean $\pm$ SD	P value
Number in each group, n	10	10	
Sex (M:F), n	4:6	5:5	0.5
Age (years)	35.8 $\pm$ 9.4	34.8 $\pm$ 12.0	0.839
BMI (kg/m <sup>2</sup> )	23.2 $\pm$ 3.0	23.9 $\pm$ 2.5	0.621
Operative time (minutes)	226 $\pm$ 32.1	209 $\pm$ 22.3	0.186
Fentanyl (micrograms)	167.5 $\pm$ 66.7	185.0 $\pm$ 70.9	0.577

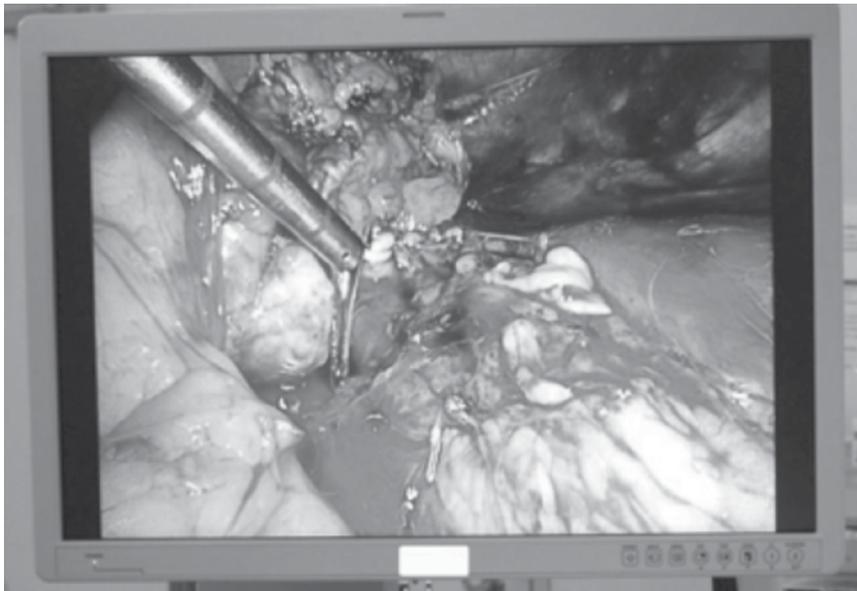
**Table 2.** Data of postoperative pain

	Normal Saline	Bupivacaine	P Value
<b>Pain score</b>			
• at first pain, median (range)	5 (2-8)	4 (2-10)	
• at first analgesic requirement, median (range)	5 (3-8)	4 (3-10)	
<b>Time</b>			
• to first pain, mean $\pm$ SD (minutes)	70 $\pm$ 44.5	165.0 $\pm$ 372.7	0.529
• to first analgesic requirement, mean $\pm$ SD (minutes)	117.0 $\pm$ 112.2	235.5 $\pm$ 364.5	0.796



**Figure 1.**

Laparoscopic live donor nephrectomy was performed with 3 ports.



**Figure 2.**

The agent was instilled at the renal bed. (2A-operative field, 2B-instrument)

(2A)



(2B)

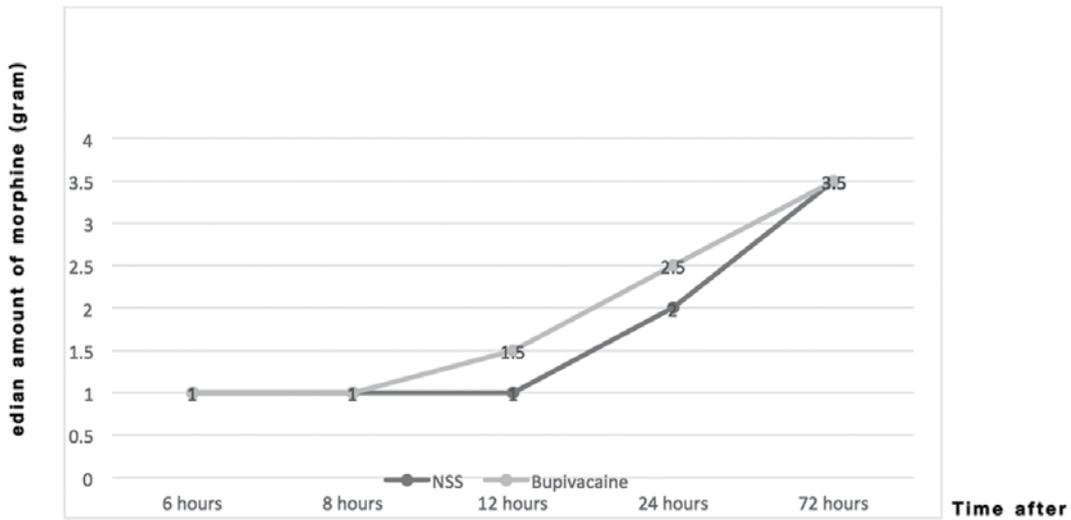


Figure 3. Comparison of oral acetaminophen usage.

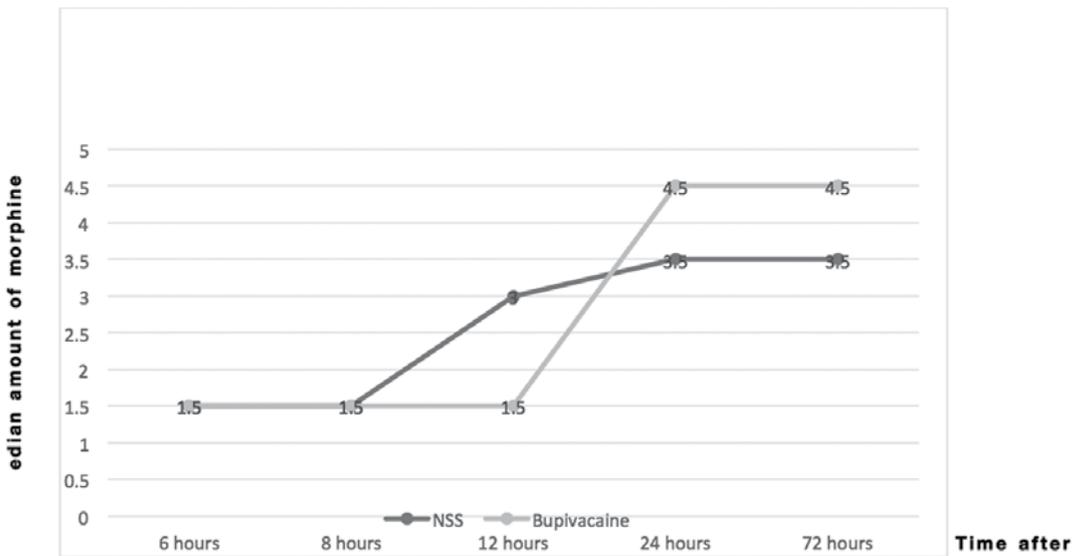


Figure 4. Comparison of parenteral morphine usage.

Fourteen of the total 20 patients, 7 in the normal saline group and 7 in the bupivacaine group, got a fever (body temperature over 37.8°C) postoperatively. All of them had a sponge bath to reduce the fever, and recovered well. There was no major complication in either group.

### Discussion

Laparoscopic live donor nephrectomy is the

standard operation for kidney donation because of its advantages: shorter hospital stays, return to work earlier, and less postoperative pain for instances. Previous study in Siriraj Hospital showed that the mean analgesic requirement in laparoscopic donor nephrectomy was lower than the requirement in the open technique ( $p < 0.001$ ).<sup>(3)</sup>

Multiple factors cause pain after laparoscopic live donor nephrectomy, such as port



wounds, incisions to retrieve the kidney, pelvic organ nociception, and peritoneal distension. Multimodalities of pain control are applied to relieve postoperative pain.<sup>(4)</sup> Nonsteroidal anti-inflammatory drugs (NSAIDs) provide moderate postoperative analgesia but are generally avoided because of their nephrotoxicity and other adverse effects, including gastrointestinal bleeding and postsurgical bleeding. The use of opioids in the postoperative period is a standard practice, but the high incidences of postoperative nausea and vomiting, respiratory depression and sedation make opioids far from the ideal analgesic drug. Epidural analgesia is used as a substitute for intravenous opioids since it has a lower incidence of postoperative nausea and vomiting, sedation, and postoperative bowel dysfunction. However epidural analgesia is associated with a lot of complications, such as urinary retention, infection at the catheter site, hypotension, lower extremity motor blockage, pruritus, and somnolence. Instillation of the local anesthetic drugs becomes a promising method because of fewer systemic adverse effects. Intra-peritoneal bupivacaine instillation has been studied to determine whether it reduced postoperative pain and analgesic usage. Despite some studies showing non-significant results, it has been used in many laparoscopic procedures, such as laparoscopic cholecystectomy and laparoscopic sterilization, to reduce pain and analgesic drugs significantly in the postoperative period.<sup>(5-14)</sup> This method has not been reported in laparoscopic nephrectomy.

This study shows that bupivacaine instillation at the renal bed tends to reduce early postoperative opiates. The pain scores at first pain and at the time of the first request for analgesic drugs were lower

in the bupivacaine group. Moreover, the patients in the normal saline group required more parenteral morphine while the patients in the bupivacaine group required more oral acetaminophen at postoperative 12 hours.

The results from this study represented that the patients in the normal saline group had higher pain scores than the patients in the bupivacaine group during the early postoperative period. The reduction of opiate consumption caused fewer side effects, such as nausea and vomiting. However, the results failed to reach statistical significance. Our study seems to show the benefit of local anesthesia using bupivacaine instillation in terms of reducing postoperative pain scores and lowering systemic analgesic requirements in the early postoperative period. Due to the short acting duration of bupivacaine<sup>(15)</sup>, our results showed higher analgesic usage in the bupivacaine groups after 12 hours, although this finding is not statistically significant. Thus, a multimodal approach seems to be beneficial in treating postoperative pain.

Since this is a pilot study, there were not enough patients recruited to demonstrate the differences between the groups. More participants are required to prove the results valid.

## Conclusion

Bupivacaine instillation at the renal bed in patients undergoing laparoscopic live donor nephrectomy tends to reduce analgesic usage in the early postoperative period. The pain score at first pain was lower in the bupivacaine group. In addition, the time to first pain and to the first analgesic requirement were longer in the bupivacaine group.

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