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# Comparison of Acute and Chronic Pain after Open Nephrectomy versus Laparoscopic Nephrectomy

## A Prospective Clinical Trial

Isik Alper, MD and Esra Yüksel, MD

**Abstract:** We evaluated postoperative pain intensity and the incidence of chronic pain in patients with renal cell carcinoma undergoing laparoscopic or open radical nephrectomy.

In this prospective study, 27 laparoscopic nephrectomy (Group LN) and 25 open nephrectomy (Group ON) patients were included. All patients received paracetamol infusion and intramuscular morphine 30 minutes before the end of the operation and intravenous patient-controlled analgesia with morphine postoperatively. Data including patients' demographics, visual analog scale (VAS) pain scores at postoperative 0.5, 1, 2, 4, 6, 12, and 24 hours, postoperative morphine consumption, analgesic demand, analgesic delivery, number of patients requiring rescue analgesics, side effects because of analgesic medications, and overall patient satisfaction were recorded and compared between the two groups. Two and 6 months after the operation, patients were evaluated for chronic postsurgical pain (CPSP).

Postoperative average VAS pain scores were not different between the two groups. However, only at 2 hours postoperatively, pain score was significantly higher in Group ON than in Group LN. In both groups, the highest pain scores were recorded at 30 minutes and 1 hour after surgery. Ninety-six percent of group ON patients and 88% of group LN patients required additional analgesia in the early postoperative period ( $P=0.33$ ). Postoperative morphine consumption and analgesic demand were found to be similar between the two groups. CPSP at 2 months after surgery was observed in 4 out of 25 patients (16%) in the ON group and 3 out of 27 patients (11.1%) in the LN group ( $P=0.6$ ). Chronic pain at 6 months after surgery was observed in 1 ON patient (4%) and 1 LN patient (3.7%,  $P=0.9$ ).

This study demonstrated that postoperative acute pain scores were not different after laparoscopic or open nephrectomy and patients undergoing laparoscopic or open nephrectomy were at equal risk of developing CPSP. Pain control should be carefully planned in order to reduce early postoperative pain and also potentially prevent CPSP.

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**Abbreviations:** CPSP = chronic postsurgical pain, DEL = delivery, DEM = demand, IV = intravenous, PACU = postanesthesia care unit, PCA = patient-controlled analgesia, RCC = renal cell carcinoma, VAS = visual analog scale.

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From the Ege University School of Medicine, Department of Anesthesiology and Reanimation, Bornova, Izmir, Turkey.

Correspondence: Isik Alper, Ege University School of Medicine, Izmir, Bornova, Turkey (e-mail: i.alper@yahoo.com).

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## INTRODUCTION

Renal cell carcinoma (RCC) accounts for 2% to 3% of all cancers and is the third most common malignancy of the genitourinary tract.<sup>1</sup> Open nephrectomy has been accepted as the standard curative treatment for resectable renal tumors for many years. With the advance of minimally invasive surgery, laparoscopic nephrectomy has become a feasible treatment alternative for localized RCC.<sup>2</sup> Studies comparing open and laparoscopic nephrectomy reported that laparoscopic nephrectomy facilitated a faster recovery and produced less pain.<sup>3</sup> However, some patients undergoing laparoscopic nephrectomy still experienced postoperative pain requiring parenteral opioids.<sup>4</sup>

The physiopathology of acute surgical pain is explained as the pain mediated by inflammatory cell infiltration, activation of the pain pathways in spinal cord, and the reflexive muscle spasm.<sup>5</sup> All of the three mechanisms of acute pain are typically ameliorated during the postoperative recovery. In some cases, persistence of the previous experience of pain and activation of pain pathways lead to postsurgical chronic pain.<sup>6</sup> Chronic postsurgical pain (CPSP) is defined as pain that develops after surgery and lasts at least for 2 months postoperatively.<sup>7</sup> The best predictive factor for CPSP is the type of surgical procedure and little is known about the progress of persistent pain after nephrectomy.

In this prospective clinical trial, we evaluated acute postoperative pain intensity and the incidence of chronic pain in patients undergoing laparoscopic or open radical nephrectomy.

## METHODS

This prospective study was conducted in 52 ASA I-II patients, aged 18 to 60 years, who were scheduled for nephrectomy. Ethical approval was provided by the Ethics Committee of Ege University School of Medicine and all of the patients gave written informed consent. Patients <18 and >60 years of age, those with known hypersensitivity to certain medicines, addicted to drugs or alcohol, or those who have an uncontrolled chronic disease were excluded from the study. In the laparoscopic group, conversion to open surgery was also taken as a criterion for exclusion.

In the evening before the operation, all of the patients were given information on how to use the patient controlled analgesic pump (PCA) and pain assessment with the visual analog scale (VAS; values 0–10; no pain to worst imaginable pain).

Patients were divided into two groups according to the planned type of operation as laparoscopic (Group LN) or open nephrectomy (Group ON). No premedication was given. In the operating room, routine monitoring was carried with electrocardiogram and noninvasive blood pressure and pulse oximeter in all patients. All patients received intravenous (IV) anesthesia through a 16-gauge IV cannula. Anesthesia induction was performed with 2 mg/kg propofol, 1 µg/kg fentanyl followed

by 0.6 mg/kg rocuronium given for neuromuscular blockage. After intubation, anesthesia was maintained with 1% to 2% sevoflurane in 40% O<sub>2</sub> and 60% air mixture. Remifentanyl and rocuronium were infused intermittently as needed. For Group LN, pneumoperitoneum was established by carbon dioxide insufflations with limiting pressure to 12 mm Hg. All patients received intravenous 1 g paracetamol infusion and intramuscular 0.1 mg/kg morphine 30 minutes before the end of the operation. Having the standard criteria for extubation, all patients were extubated in the operating room and transferred to the postanesthesia care unit (PACU).

All the patients received intravenous morphine patient-controlled analgesia (PCA) postoperatively after arrival to PACU. PCA was set on the demand mode without a loading dose. The dose of morphine was set at 0.02 mg/kg with a time-lock interval of 15 minutes. The additional analgesic (1.5 mg/kg tramadol IV) was given if the VAS score was >4 over 15 minutes. During the postoperative period at 0.5, 1, 2, 4, 6, 12, and 24 hours after arrival to the PACU, patients were assessed for VAS pain scores, SpO<sub>2</sub>, heart rate (HR), and mean blood pressure (MBP). Postoperative morphine consumption, analgesic demand (DEM) and delivery (DEL), and number of patients requiring additional analgesic were recorded and compared between the two groups. Analgesic-related side effects were specifically observed and recorded for a period of 24 hours, including nausea, vomiting, hypotension, bradycardia, allergic reactions, drowsiness, paresthesia, and respiratory depression. At the end of the study, the overall patient satisfaction degree was questioned and divided as the following: 5 = excellent, 4 = good, 3 = moderate, 2 = poor, and 1 = bad.

Two and 6 months after the operation, patients were called and asked whether they experience pain in the incision area and positive responses were recorded as chronic pain.

Statistical analysis was performed using a computer-based statistical program. The normally distributed data were compared using the independent *t* test. The Mann-Whitney *U* test was used for postoperative VAS pain scores and the chi-square test was used for analgesic demands between two groups. The level of statistical significance was set at  $P < 0.05$ .

## RESULTS

A total of 52 patients who underwent nephrectomy were studied. Twenty-seven patients had laparoscopic nephrectomy (Group LN) and 25 had open nephrectomy (Group ON). Demographic characteristics as the duration of anesthesia and surgery were similar between the two groups (Table 1).

Perioperative average of total remifentanyl dose was not different between Group ON and Group LN (21.4 + 8.4 mL and 23 + 12 mL, respectively;  $P = 0.56$ ).

**TABLE 1.** Demographic Characteristics, Duration of Anesthesia and Surgery

	Group ON	Group LN	<i>P</i>
Age (year)	53.6 ± 15.4	53.7 ± 14.7	0.98
BMI (kg/m <sup>2</sup> )	26.3 ± 4.9	28.9 ± 3.4	0.99
Duration of anesthesia (min)	152 ± 36	171 ± 46	0.09
Duration of surgery (min)	135 ± 35	150 ± 35	0.13

Values are presented as mean ± SD.

BMI = body mass index, Group LN = laparoscopic nephrectomy group, Group ON = open nephrectomy group.

**TABLE 2.** Postoperative Pain Scores (VAS)

	Group ON	Group LN	<i>P</i>
VAS 30 min	8.3 ± 1.8	7.4 ± 2.02	0.07
VAS 1 h	6.7 ± 2.2	5.8 ± 1.6	0.09
VAS 2 h	5.1 ± 2.7	3.5 ± 2.3*	0.02
VAS 4 h	3.2 ± 2.0	2.1 ± 2.0	0.08
VAS 6 h	1.5 ± 1.8	0.8 ± 1.4	0.13
VAS 12 h	0.6 ± 1.2	0.1 ± 0.5	0.08
VAS 24 h	1.4 ± 2.1	1.0 ± 1.9	0.43

Values are presented as mean ± SD.

Group LN = laparoscopic nephrectomy group, Group ON = open nephrectomy group, VAS = visual analog scale.

\* $P < 0.05$ .

Postoperative average VAS pain scores were not different between the two groups. However, only at 2 hours postoperatively, VAS pain score was significantly higher in Group ON compared with Group LN (Table 2). In both groups the highest pain scores were recorded at 30 minutes and 1 hour after surgery. In the early postoperative period, 96% of group ON patients and 88% of group LN patients required additional analgesia ( $P = 0.33$ ). Postoperative morphine consumption, DEM, and DEL were found to be similar (Table 3).

Chronic pain at 2 months after surgery was observed in 4 out of 25 patients (16%) in Group ON and 3 out of 27 patients (11.1%) in Group LN ( $P = 0.6$ ). Six months after surgery, CPSP was observed in 1 ON patient (4%) and 1 LN patient (3.7%;  $P = 0.9$ ).

Two patients in Group ON and 1 patient in Group LN reported nausea and vomiting. Patient satisfaction was found to be similar between the two groups ( $P = 0.143$ ) (Table 4).

## DISCUSSION

We evaluated postoperative pain intensity and the incidence of chronic pain in patients with RCC undergoing open and laparoscopic nephrectomy. Postoperative pain scores were found to be similar between the laparoscopic and open nephrectomy patients. However, only at 2 hours postoperatively, VAS scores were significantly higher in Group ON than in Group LN. The highest pain scores were recorded at 30 minutes and 1 hour after surgery within the both groups. The incidence of chronic pain at 2 and 6 months after surgery was found similar for the two groups.

Although much progress had been seen in anesthesia and surgical techniques, such as minimal invasive procedures, many

**TABLE 3.** Postoperative Morphine Consumption, Analgesic Demand and Delivery

	Group ON	Group LN	<i>P</i>
Postoperative morphine consumption (mg)	16.2 ± 3.8	17.1 ± 6.8	0.56
Analgesic delivery (mL)	12.4 ± 9.5	8.4 ± 2.0	0.52
Analgesic demand (mL)	40.8 ± 28.7	37.9 ± 23.3	0.68

Values are presented as mean ± SD.

Group LN = laparoscopic nephrectomy group, Group ON = open nephrectomy group.

**TABLE 4.** Patients' Satisfaction (5 = Excellent, 4 = Good, 3 = Moderate, 2 = Poor, 1 = Bad)

	2	3	4	5
Group ON	2	12	11	
Group LN	1	8	14	4

Values are presented as number of patients.

Group LN = laparoscopic nephrectomy group, Group ON = open nephrectomy group.

patients still experience severe postoperative pain and related complications. Studies comparing open and laparoscopic nephrectomy reported that laparoscopic surgery has some advantages with regard to perioperative morbidity, including blood loss, postoperative analgesic requirement, duration of hospitalization, and recovery.<sup>8,9</sup> Andersen et al have compared open versus laparoscopic donor nephrectomy to evaluate postoperative pain and convalescence in a prospective, controlled trial and reported a significant difference in favor of the laparoscopic group regarding administered analgesics on the day of surgery. Postoperative morphine requirement was found to be  $14.5 \pm 8.7$  mg versus  $18.6 \pm 9.9$  mg for laparoscopic versus open nephrectomy patients, respectively. However they did not find any difference between groups regarding self-reported pain on the second postoperative day as VAS scores were similar for both groups.<sup>10</sup> Studies that evaluated pain following open and laparoscopic nephrectomy reported that analgesic requirement was significantly lower in the laparoscopic group.<sup>9</sup> Bachmann et al found that laparoscopic nephrectomy combined with paracetamol and subcutaneous administration of opiates resulted in sufficient analgesia, thus permitting earlier mobilization increasing the overall well-being after surgery.<sup>11</sup> On the other hand, it is reported that some patients undergoing laparoscopic nephrectomy still experienced postoperative pain requiring parenteral opioids.<sup>3,4</sup> Pain at the inner surgical site, laparoscopic port sites and incision, organ nociception, and ureteric colic together with urinary tract discomfort associated with urinary catheter contributed to the postoperative pain and some patients might require more analgesics compared with those having open nephrectomy.<sup>4</sup>

In our study, acute postoperative average pain scores were not different between the laparoscopic and open nephrectomy patients. The difference reached significance only at one time point (2 hours postoperatively) between the groups. The higher pain scores were found especially in the early postoperative period for both groups and adequate pain relief was achieved at 2 hour for laparoscopic nephrectomy patients and at 4 hour for open nephrectomy patients postoperatively. We also found that more patients in the ON Group needed additional analgesia compared with the LN Group, although the difference was not statistically significant. We administered intravenous 1 g paracetamol infusion and intramuscular 0.1 mg/kg morphine 30 minutes before the end of the operation as our routine practice. However, intramuscular administration of morphine can be the reason of higher pain scores in the early period in both groups, because of the time delay between morphine administration and analgesic effect. This may also contributed to the similar pain scores between the groups.

Inadequately controlled pain has a wide spectrum of effects on the body. It had been reported that poorly controlled acute postoperative pain may result in chronic pain.<sup>12</sup> CPSP is a

largely unrecognized problem that may occur in 10% to 65% of postoperative patients depending on the type of surgery, with 2% to 10% of these patients experiencing severe CPSP.<sup>13</sup> Although much research has been done to determine the incidence and risk factors of CPSP in different surgical procedures, little is known about the progress of persistent pain after nephrectomy.<sup>14</sup>

One month after nephrectomy pain has been reported in 58% and 78% of patients in two different studies.<sup>10,15</sup> However, in these studies, patients were donors. The International Association for the Study of Pain (IASP) defined chronic pain as lasting >6 months for chronic pain of non-tumor origin and >3 months for cancer pain.<sup>16</sup> Following this definition, the incidence of CPSP after open nephrectomy ranges from 4% to 27%.<sup>17</sup>

In our study, we found the incidence of chronic pain after open nephrectomy to be 16% at 2 months and 4% at 6 months which is in line with the literature and also the incidence of CPSP was similar for both open and laparoscopic nephrectomy patients at 2 and 6 months after surgery. However, the statistical results for CPSP are limited by the small number of patients in this study.

Although the role of acute postoperative pain intensity in the development of CPSP is not fully understood, the severity of acute postoperative pain may be an important predictor in the development of CPSP.<sup>18</sup> One other factor in predicting the development of CPSP may be the severity of the patient's preoperative pain.<sup>19</sup> Patients with more intense levels of preoperative pain may also develop a degree of CNS sensitization predisposing them to the increased likelihood of higher postoperative pain and the subsequent development of chronic pain.<sup>19</sup> This is one of the limitations of our study since we couldn't make a careful preoperative examination to assess existing pain conditions in the surgical field.

In conclusion, this study demonstrated that acute postoperative average pain scores were not different between the patients undergoing laparoscopic or open nephrectomy. The highest pain scores were recorded at 30 minutes and 1 hour after surgery in both groups. Patients undergoing laparoscopic or open nephrectomy carried equal risk for developing chronic pain. Pain control should be carefully planned in order to reduce early postoperative pain and also potentially prevent CPSP.

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