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# Is the amount of carbon dioxide gas used in urologic laparoscopic surgeries associated with postoperative pain?

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**Purpose:** We measured how much $CO_2$ gas was used in urologic laparoscopic surgeries and studied whether the amount of gas was associated with postoperative pain.
**Materials and Methods:** Four hundred sixty-three patients underwent urologic laparoscopic surgeries by a single surgeon. All surgeries were performed by a transperitoneal approach under a 15-mm Hg pneumoperitoneum using $CO_2$ gas. The amount of $CO_2$ was measured. Neuromuscular blockade with rocuronium was performed during the surgery and patient-controlled analgesia was also applied. Postoperative pain was assessed four times for 24 hours using a 10-point visual analogue scale.
**Results:** The mean laparoscopic time was 75.65±38.19 minutes and the mean amount of $CO_2$ gas used was 415.70±190.68 L. The mean score on the postoperative pain scale was 6.37±1.48 for 12 hours (sum of measurements taken at 6 and 12 hours after the surgery) and 11.72±2.46 for 24 hours (sum of measurements at 6, 12, 18, and 24 hours). In the statistical analysis, there were no correlations between the amount of $CO_2$ used and pain scores for 12 and 24 hours postoperatively. There were no correlations between laparoscopic time and pain scores for 12 or 24 hours postoperatively. There were also no correlations between operative method and pain scores for 12 or 24 hours postoperatively.
**Conclusions:** We recorded the amount of $CO_2$ gas used for each laparoscopic surgery. There was no correlation between the amount of $CO_2$ used and postoperative pain. The lack of correlation may have been because the surgery was performed under anesthesia with deep neuromuscular blockade.

**Keywords:** Carbon dioxide; Laparoscopy; Pain; Pneumoperitoneum



## INTRODUCTION

Laparoscopic surgeries including robotics are increasing rapidly in the field of urology. Although rapid developments have been made in instruments and machines, there have been no changes in the process of creating pneumoperitoneum. Production of pneumoperitoneum with carbon dioxide ($CO_2$) gas is essential in all laparoscopic surgery, and various amounts of gas are used depending on the surgical procedure. Urologists need to know how much $CO_2$ has to be pre-

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pared for the surgery. However, it is not known exactly how much gas is used in urologic laparoscopic surgery.

We know that laparoscopic surgery is less invasive, and one of the advantages of less invasive surgery is less pain [1]. However, laparoscopic surgery also has postoperative pain [2]. It is known that $CO_2$ can cause cardiovascular and respiratory disorders as well as postoperative pain. Although the causes of pain are various, several papers have stated that the accumulated gas in the body stimulates the diaphragm and causes shoulder pain. However, it is not known whether $CO_2$ really causes pain and whether the amount of gas used is associated with pain.

We therefore measured how much $CO_2$ gas was used in urologic laparoscopic surgeries and studied whether the amount of gas is associated with postoperative pain.

## MATERIALS AND METHODS

This study was approved by Wonkwang University Hospital Institutional Review Board (approval number: 1530). Written informed consent was omittable and the omission was also approved. We reviewed the records of 595 patients who underwent laparoscopic surgeries for upper urinary tract diseases between April 2014 and March 2019. All operations were performed by a single surgeon using a transperitoneal approach. Of the patients studied, 463 patients (58 cases of adrenalectomy, 70 cases of renal cyst excision, 59 cases of pyeloplasty, 31 cases of simple nephrectomy, 95 cases of partial nephrectomy, 84 cases of radical nephrectomy, and 66 cases of nephroureterectomy) were enrolled in this study. The mean age of the 267 men and 196 women was 60.57±13.99 years, and the mean height and body weight were 161.11±12.44 cm and 67.02±34.74 kg, respectively. The mean of American Society of Anesthesiologists (ASA) Physical Status Classification score was 1.49±0.56 [3].

All laparoscopic surgeries were performed under a 15-mm Hg pneumoperitoneum using $CO_2$ gas, induction with a high flow rate (10 L/minute), and maintenance with a low flow rate (1 L/minute). The amount of $CO_2$ gas used was measured. The amount of $CO_2$ gas was measured from the point of connecting the $CO_2$ gas after puncture with the Veress needle to the point of turning off the $CO_2$ at the end of the surgery. The anesthesiologists monitored invasive, partial pressure of arterial carbon dioxide (Pa $CO_2$) and noninvasive, end-tidal $CO_2$ (Et $CO_2$) in the mechanically ventilated patients. They adjusted the respiratory rate considering the difference. The Et $CO_2$ was maintained at 35 to 40 mm Hg. Finally, any significant hypercapnia was controlled using minute ventilation. Anesthesia with deep neuromuscular blockade (NMB) in laparoscopy was performed according to our own principle. Rocuronium 0.6 mg/kg, a neuromuscular blocking agent, was administered at induction of anesthesia and an additional dose of 0.2 mg/kg was given according to the train-of-four (TOF) ratio and titrated toward a post-tetanic count of 1 to 3 during maintenance of anesthesia. Reversal of NMB at extubation was performed by administering sugammadex 4 mg/kg.

A patient-controlled analgesia pump containing fentanyl (800 μg), ketorolac (60 mg), and ramosetron (0.6 mg) in a total volume of 100 mL of saline was set to deliver a basal infusion of 2 mL/h and bolus doses of 0.5 mL, with a 15-minute lockout period for postoperative analgesia. Postoperative pain intensity was assessed using a 100-mm linear visual analogue scale, which was classified from 1 to 10. The pain scores were measured every 6 hours for 24 hours after laparoscopy. Postoperatively, arterial blood gas analysis was performed.

Statistical analysis was done to determine whether the amount of $CO_2$ gas used for surgery was related to the postoperative pain. Accordingly, a p-value of $<0.05$ was considered significant. IBM SPSS Statistics for Windows version 19.0 (IBM Corp., Armonk, NY, USA), was used in all statistical analyses.

## RESULTS

The mean laparoscopic time was 75.65±38.19 minutes (48.36±20.59 minutes for adrenalectomy, 34.68±17.68 minutes for renal cyst excision, 90.95±41.51 minutes for pyeloplasty, 82.97±32.52 minutes for simple nephrectomy, 82.20±36.05 minutes for partial nephrectomy, 92.73±32.42 minutes for radical nephrectomy, and 95.58±29.40 minutes for nephroureterectomy), and the mean amount of $CO_2$ gas used was 415.70±190.68 L (299.90±116.44 L for adrenalectomy, 205.63±115.29 L for renal cyst excision, 466.31±176.13 L for pyeloplasty, 418.22±150.55 L for simple nephrectomy, 446.97±186.61 L for partial nephrectomy, 505.85±152.27 L for radical nephrectomy, and 537.98±158.85 L for nephroureterectomy) (Table 1). There was a statistically significant correlation between surgical method and $CO_2$ amount using the Pearson correlation coefficient (p=0.009). Change in postoperative pain intensity was measured four times for 24 hours after laparoscopy. The mean postoperative pain score was 6.37±1.48 for 12 hours (the sum of measurements taken at 6 and 12 hours after the surgery) and 11.72±2.46 for 24 hours (the sum of measurements at 6, 12, 18, and 24 hours). The mean of each of the four measurements was measured, and the mean of all the sums was 2.96±0.63. The pain score was highest at 6 hours post-

Table 1. Amount of $CO_2$ used and postoperative pain by type of laparoscopic surgery

| Type of laparoscopy | No. of patients | Laparoscopic time (min) | $CO_2$ amount (L) | Postoperative pain score (point) | | |
|---|---|---|---|---|---|---|
| | | | | 12 hours[a] | 24 hours[b] | Sum[c] |
| Adrenalectomy | 58 | 48.36±20.59 | 299.90±116.44 | 6.41±1.64 | 11.63±2.33 | 2.99±0.64 |
| Renal cyst excision | 70 | 34.68±17.68 | 205.63±115.29 | 6.27±1.32 | 11.51±2.11 | 2.90±0.52 |
| Pyeloplasty | 59 | 90.95±41.51 | 466.31±176.13 | 6.31±1.50 | 11.00±2.46 | 2.78±0.64 |
| Simple nephrectomy | 31 | 82.97±32.52 | 418.22±150.55 | 6.16±1.70 | 11.80±2.30 | 2.95±0.75 |
| Partial nephrectomy | 95 | 82.20±36.05 | 446.97±186.61 | 6.52±1.50 | 11.80±3.04 | 3.00±0.61 |
| Radical nephrectomy | 84 | 92.73±32.42 | 505.85±152.27 | 6.42±1.62 | 12.09±2.70 | 3.04±0.68 |
| Nephroureterectomy | 66 | 95.58±29.40 | 537.98±158.85 | 6.33±1.17 | 12.00±2.39 | 3.00±0.59 |
| Total | 463 | 75.65±38.19 | 415.70±190.68 | 6.37±1.48 | 11.72±2.46 | 2.96±0.63 |

Values are presented as number only or mean±standard deviation.
[a]:12 hours is the sum of scores at 6 and 12 hours after surgery. [b]:24 hours is the sum of scores at 6, 12, 18, and 24 hours after surgery. [c]:Sum is the mean of each of the four measurements.

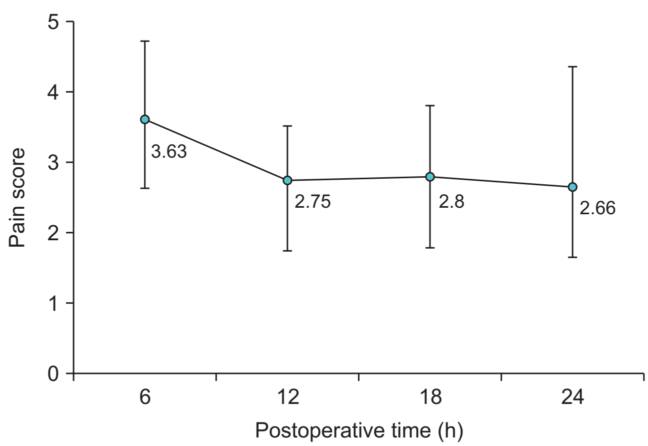


Fig. 1. Postoperative pain score (mean±standard deviation) after laparoscopy.

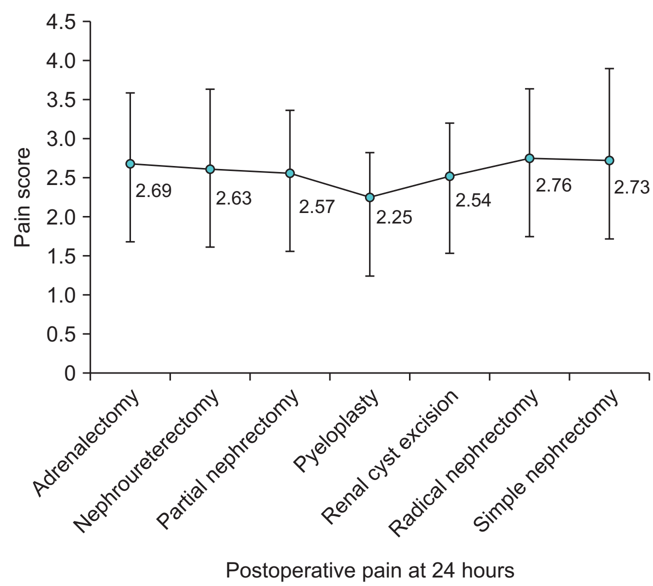


Fig. 3. Pain score (mean±standard deviation) at 24 hours after several types of laparoscopies.

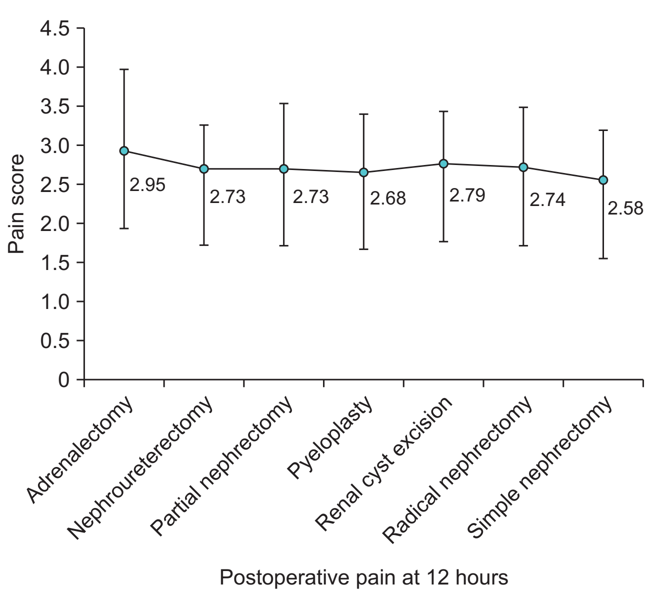


Fig. 2. Pain score (mean±standard deviation) at 12 hours after several types of laparoscopies.

operatively and decreased from 12 hours to 24 hours (Fig. 1). In terms of pain intensity at 12 and 24 hours after surgery, there was no significant difference in postoperative pain according to the type of laparoscopic surgery (Figs. 2, 3).

In the statistical analysis using the independent t-test, there were no significant correlations between the amount of $CO_2$ gas used and pain scores for 12 hours (p=0.203) or 24 hours (p=0.784) postoperatively. There were also no significant correlations between the $CO_2$ amount and postoperative pain score at each time point (p=0.988). In the statistical analysis using the independent t-test, there were no significant correlations between laparoscopic time and pain scores for 12 hours (p=0.554) or 24 hours (p=0.554) postoperatively. There was also no correlation with pain score at each time point (p=0.576). The correlations between type of laparoscopy

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and pain scores for 12 hours (p=0.908) or 24 hours (p=0.228) postoperatively were not statistically significant (one-way ANOVA test). There was also no correlation with pain score at each time point (p=0.245).

## DISCUSSION

The use of laparoscopic or robotic surgery is rapidly increasing in the field of urology, and $CO_2$ is fundamental for creating the pneumoperitoneum. Although $CO_2$ is the most commonly used gas, no previous research has examined the amount of gas used in laparoscopic surgery. We measured the amount of $CO_2$ used in various types of laparoscopic surgery for upper urinary tract diseases. Our results suggest that an appropriate amount of $CO_2$ should be prepared to complete the surgery.

$CO_2$ has the advantages of being inexpensive, colorless, noncombustible, and chemically stable. The gas is highly soluble in blood and can easily diffuse in body tissues. Owing to the physiologic characteristics of the gas, there is the possibility of the gas causing some complications. The rapid absorption can lead to cardiovascular, renal, and pulmonary dysfunction. It can also induce other complications from abdominal insufflation [4]. Although laparoscopic surgery is less invasive than open surgery, it also has postoperative pain.

Although the pain is mild to moderate, pain in the abdomen and shoulder has been reported after laparoscopic abdominal surgery. The incidence of postoperative pain after gynecologic laparoscopies has been reported to vary from 35% to 63% [5,6]. In particular, shoulder pain after laparoscopic cholecystectomy has been reported in 30% to 50% of cases [7,8]. In some studies, up to 80% of patients undergoing laparoscopic cholecystectomy were managed with opiates postoperatively [9]. Interestingly, Ekstein et al. [2] showed that among patients with severe pain immediately after abdominal surgery, laparoscopic surgery accounted for 46% of patients, and the intensity of pain was stronger and more analgesics were needed in those patients than for patients who underwent open surgery. By 24 hours, the former were in less pain than the latter. In our study, most of the patients who underwent laparoscopic surgery complained of postoperative pain. Pain was most severe at 6 hours postoperatively and decreased from 12 to 24 hours postoperatively.

The cause of postoperative pain is multifactorial and complex. Pain intensity is associated with the location of the surgery and its extent; the degree of tissue traumatization, including the direction of the skin incision; the patient's preoperative anxiety level; and the analgesic techniques used in the perioperative period. However, unlike open surgery, $CO_2$ insufflation is widely assumed to be responsible for the pain. It has been hypothesized that the gas induces morphologic and biochemical changes and expands and stimulates the diaphragm and peritoneum [10-12]. Retained $CO_2$ in the abdomen is thought to be a major mechanism of shoulder pain. The gas irritates the phrenic nerve and as a result causes referred pain in the C4 dermatome [10,13]. In other words, the stretched diaphragm leads to phrenic neuropraxia, typically recognized as shoulder pain [14,15]. This also causes abdominal pain because the carbon dioxide trapped between the liver and the right diaphragm stimulates the diaphragm [16,17]. In genetic studies, it has been hypothesized that the pneumoperitoneum, made of $CO_2$, can adversely affect the gene expression of extracellular matrix, adhesion, and inflammatory cytokine signal molecules in peritoneal tissue [18]. As a result, increased peritoneal seeding, peritoneal tissue hypoxia, and postoperative adhesion formation have been demonstrated in animal studies [19,20]. Those studies suggested that $CO_2$ has an adverse impact on the surgical peritoneal situation and postoperative clinical consequences, including pain.

Although the mechanism of pain after laparoscopy is not clear, pain makes the patient uncomfortable and is worthy of intervention. Under the assumption that the carbon dioxide used in laparoscopic surgery is a key factor in pain, various efforts have been made to decrease pain in patients undergoing laparoscopic surgery. Several studies have shown that low pressure can reduce postoperative pain [6,21,22]. Low intraperitoneal pressure (IPP) of 8 to 9 mm Hg results in a decrease in the frequency and severity of shoulder pain postoperatively. In particular, Ferroni and Abaza [23] showed that ultra-low pneumoperitoneum of 6 mm Hg may confer a pain benefit in robot-assisted laparoscopic prostatectomy. Those authors showed that ultra-low pneumoperitoneum improves quality of life in the early stages of postoperative rehabilitation and reduces hospitalization. Matsuzaki et al. [18] suggested that inflammation is reduced in patients undergoing laparoscopic subtotal hysterectomy with a low IPP of 8 mm Hg compared with standard IPP (12 mm Hg), resulting in better clinical results. They showed lower postoperative pain at 12 and 24 hours using visual analogue pain scores. Expression of inflammation-related genes in peritoneal tissues was significantly reduced at low IPP.

If residual carbon dioxide is washed away or removed, the frequency or intensity of postoperative pain will be reduced. Although there was little evidence of reduced pain after intraperitoneal gas drainage, Tharanon and Khampitak [24] attempted intraperitoneal gas release for 48 hours to reduce overall postoperative pain in gynecologic laparoscopic surgery. This result was more effective in patients with longer operative times (more than 2 hours). Using the property of $CO_2$ to dissolve in water, Tsai et al. [25] tried intraperitoneal normal saline infusion to eliminate $CO_2$ from the intraperitoneal space. They filled the upper part of the intraperitoneal cavity with isotonic normal saline and removed the trocars, leaving the saline in place. Abdominal and shoulder pain were significantly decreased at 24 and 48 hours after laparoscopic surgery for gynecologic diseases. Intraperitoneal normal saline infusion may have acted as a physiologic buffer system that promotes the disappearance of the intraperitoneal $CO_2$ and consequently prevents irritation of the diaphragm [26]. The result would be less abdominal and shoulder pain after surgery. In a more proactive manner, intraperitoneal administration of local anesthetics has been attempted. Injection of 0.5% bupivacaine into the diaphragmatic area was shown to reduce shoulder pain and finally analgesic consumption [7,8]. Recently, ropivacaine has been used. Administration of 3.75% ropivacaine before and after laparoscopic cholecystectomy was shown to be effective for decreasing the postoperative pain and stress response [27].

Since $CO_2$ gas plays an important role in pain after laparoscopic surgery, much effort has been made to lower the pressure, quickly remove the gas, neutralize it, and eliminate irritation. However, in our study, the amount of $CO_2$ used and postoperative pain were not related. We maintained the IPP at 15 mm Hg when performing laparoscopic surgery and administered neither intraperitoneal saline nor local anesthetics. However, the amount of $CO_2$ was not associated with pain scores for 12 or 24 hours after surgery. The reason for the lack of correlation between $CO_2$ amount and postoperative pain was that the anesthesiologist appropriately controlled and treated pain during and after the surgery. In particular, NMB might have an important role in decreasing pain.

There are some suggestions that NMB may help to reduce pain during surgery because deep NMB allows laparoscopic surgery without muscle tension in the abdominal wall or diaphragm. It supports complete paralysis of the muscles of the abdominal wall and diaphragm. A deep level of NMB can also reduce the pressure required to achieve the same degree of peritoneal insufflation. Madsen et al. [28] showed that the incidence of shoulder pain is remarkably reduced after deep-to-intense NMB in patients who undergo laparoscopic hysterectomy. In that study, the risk of shoulder pain was absolutely reduced by 31% with the combination of deep NMB using administration of rocuronium under low-pressure pneumoperitoneum. This decrease was seen within the first 3 days after surgery. Castro et al. [29] showed that sugammadex combined with deep NMB reduces pain after laparoscopic bariatric surgery. They reported that visual analogue pain scores were lower at 30 and 60 minutes after arrival in the post-anesthesia care unit.

We used deep NMB with rocuronium that was reversed with sugammadex for patients who underwent laparoscopy for urinary tract disease. Rocuronium has a rapid onset of action that appropriates succinylcholine, making it a suitable alternative for rapid sequence induction, and sugammadex selectively bonds to the rocuronium to make deep NMB. As a result, there was no difference in postoperative pain regardless of $CO_2$ usage. There was also no correlation between the method and time of surgery and postoperative pain. Even if a large amount of $CO_2$ is used for laparoscopic surgery, it can be assumed that postoperative pain is not affected under application of NMB. However, since pain is so subjective, there is still no exact answer as to whether the use of deep NMB affects postoperative pain. This issue should be pursued in further studies.

## CONCLUSIONS

Laparoscopic surgery, although less invasive, also induces postoperative pain. This pain is known to be associated with $CO_2$ gas. Our study revealed the amount of $CO_2$ used in different types of urologic laparoscopic surgery. In addition, we measured postoperative pain in the patients undergoing the surgeries. However, there was no correlation between the amount of $CO_2$ used and the patients' postoperative pain, which was probably due to the NMB performed during the surgery. We believe that if proper pain management is performed during surgery, postoperative pain can be controlled regardless of $CO_2$ usage. However, postoperative pain may also be due to causes other than $CO_2$, so more research will be needed.

## CONFLICTS OF INTEREST

The authors have nothing to disclose.

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## AUTHORS' CONTRIBUTIONS

Research conception and design: Ill Young Seo. Data acquisition: Ill Young Seo and Tae Hoon Oh. Statistical


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analysis: Tae Hoon Oh and Cheol Lee. Data analysis and interpretation: Ill Young Seo and Cheol Lee. Drafting of the manuscript: Ill Young Seo. Critical revision of the manuscript: Ill Young Seo. Approval of the final manuscript: all authors.

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