ORIGINAL ARTICLE

Cardiovascular and Respiratory Changes and Convalescence in Laparoscopic Colonic Surgery

Comparison Between Carbon Dioxide Pneumoperitoneum and Gasless Laparoscopy

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Hypothesis: Gasless laparoscopy produces smaller cardiopulmonary and systemic changes than carbon dioxide (CO_2) laparoscopy during colonic surgery.

Design: Prospective randomized trial.

Setting: Department of Surgery in a university hospital.

Patients: Twenty-two patients scheduled for laparoscopic colonic resection; 5 patients were excluded because of conversion to open surgery (N = 17).

Interventions: Patients were randomized to either gasless (n = 9) or conventional CO_2 (n = 8) surgery.

Main Outcome Measures: Intraoperative assessment of hemodynamic factors and pulmonary function, and postoperative assessment of pain, pulmonary function, convalescence, and various injury factors were done several times until 30 days after surgery. Surgical complications were noted.

Results: Descending aorta blood flow after 30 minutes ($P = .03$) and heart rate after 150 minutes were higher in the CO_2 group ($P = .009$). Central venous pressure, Pa_{CO_2}, inspiration pressure, and end tidal CO_2 level were significantly higher in the CO_2 group ($P = .05$, .03, .04, and .01, respectively). Patients in the CO_2 group had less pain during mobilization and coughing ($P = .008$ and .006, respectively), and were significantly more fatigued ($P = .04$). No other important differences were observed in intraoperative hemodynamic factors, postoperative convalescence, immunocompetence, or pulmonary function.

Conclusion: No clinically important differences in cardiovascular and systemic response were observed between patients undergoing CO_2 or gasless laparoscopy for colonic disease.

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LAPAROSCOPY is superior to open surgery because it is accompanied by a shorter hospital stay, more rapid convalescence, less immunosuppression, and a smaller catabolic response.[1-3] However, although patients experience less pain and smaller affection of pulmonary function, significant hemodynamic changes develop in patients undergoing laparoscopy using pneumoperitoneum.[4-6] Thus, complications such as deep venous thrombosis and respiratory acidosis with subsequent risk of cardiac arrhythmias have been reported,[6-9] especially in patients with preexisting cardiac or respiratory disease.[8,10,11]

Because of these complications, other gases such as helium and nitrous oxide have been evaluated, although no obvious clinical advantage has been reported to date, to our knowledge.[4,12] Another approach may be laparoscopy without pneumoperitoneum, for which different methods of abdominal wall elevation have been developed.[13-15] These methods may improve outcome following laparoscopic surgery by decreasing the risk of especially cardiovascular complications and perhaps by smaller systemic catabolic response. Most studies considered the differences in cardiorespiratory affection,[16-18] whereas only a few focused on neuroendocrine and immunologic differences.[19,20]

The aim of this study was to perform the first prospective randomized comparison between carbon dioxide (CO_2) pneumoperitoneum and the abdominal wall lift method on cardiovascular, respiratory, and systemic response in patients undergoing laparoscopic colonic surgery.

RESULTS

Five patients were excluded because of conversion from laparoscopic to open surgery (2 in the GL group and 3 in the CO_2 group). Hence, 17 patients completed the

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PATIENTS AND METHODS

Twenty-two patients provided informed consent and entered the study, which was approved by ethics committees in Copenhagen and Frederiksberg. Patients with preoperative signs of extensive local tumor growth and those scheduled for rectal surgery were excluded. Patients were randomized to either gasless (GL) or conventional CO_2 laparoscopic operation. If an operation was converted to open surgery, those patients were excluded from the study from the time of conversion.

All patients received piroxicam sodium, 40 mg, the night before the operation and diazepam, 0.15 mg/kg, orally 1 hour before induction of anesthesia. A thoracic epidural catheter (covering T-4 to T-12) was inserted and patients were injected with morphine hydrochloride, 2 mg, followed by lidocaine hydrochloride, 9 mL (20 mg/mL), and epinephrine hydrochloride (50 μg/mL). Regional anesthesia was ensured by pinprick, then anesthesia was induced with thiopental sodium, atracurium besylate, midazolam hydrochloride, and fentanyl citrate. Anesthesia was maintained with isoflurane and epidural infusion of bupivacaine hydrochloride, 2.5 mg/mL (4 mL/h), and morphine, 0.2 mg/h (ambulatory PCA pump; Bard, North Reading, Me). Patients were ventilated with a respirator (model MCM801; Dameca, Copenhagen, Denmark) adjusted to maintain the end-tidal CO_2 ($ETCO_2$) between 4.0 and 6.0 kPa throughout the procedure. Postoperatively, the epidural infusion was continued for 48 hours and additional morphine in intramuscular doses of 5 to 10 mg was used on request.

All patients received ampicillin, 2 g; gentamicin sulfate, 240 mg; and metronidazole, 1 g, intravenously at the time of skin incision as antibiotic prophylaxis. A bladder catheter and a nasogastric tube were in place during the operation, and were removed at the end of the operation. All patients were allowed to eat solid food from the day of the operation.

For CO_2 laparoscopic procedures, pneumoperitoneum and trochars were established and placed as described previously.[21] For GL operations, retraction of the abdominal wall was achieved by the planar lifting technique (Laparolift; Oregon Medical Systems, San Jose, Calif).[15]

For intraoperative hemodynamic and respiratory evaluation, the patients were monitored continuously with electrocardiogram, arterial blood pressure, central venous pressure, and oxygen saturation, pulse-oximetry (Propaq 106; Protocol Systems, Houston, Tex), thoracic impedance (CN 953; Per Caspersen, Copenhagen, Denmark), descending aorta flow (Dynemo 3000; Sometec, Paris, France), $ETCO_2$ tension (Oscar II, Sc 123; Datex, Helsinki, Finland) and inspirational pressure (MCM 801 C; Dameca, Copenhagen, Denmark). Thoracic impedance was measured using a 4-electrode method at 100 kHz, with the electrodes placed across the thorax to estimate volume changes.[22] Following tracheal intubation but before surgery, an esophageal probe was placed with its tip approximately at the third intercostal space. The probe was equipped with both ultrasound and pulsed doppler transducers, enabling estimation of flow in the descending aorta shown to correlate with cardiac output.[23] Electrocardiogram was monitored continuously with a Holter tape recorder (model 90205; Spacelabs Inc, Washington, DC) from before administration of anesthesia to 24 hours after surgery. Central venous pressure (Propaq 106; Protocol Systems), central venous oxygen saturation and arterial blood gasses were measured prior to anesthesia (ABL 615; Radiometer, Copenhagen, Denmark) at skin incision and every 30 minutes during surgery. Esophageal temperature (DM 852; Ellab, Copenhagen, Denmark) was measured before anesthesia and at the end of surgery.

Venous blood samples were drawn on ice on the day of operation (day 0), and 1, 3, and 10 days after surgery between 8 and 10 AM for analyses of C-reactive protein (CRP), interleukin 6 (IL-6), and plasminogen activator inhibitor type 1 (PAI-1). Blood samples were separated (1800*g* for 10 minutes at 4°C), and plasma and serum were stored at −20°C until analysis; CRP and IL-6 were measured as described earlier.[24] Plasminogen activator inhibitor type 1 was analyzed using an in-house enzyme-linked immunosorbent assay technique[25] with detection limit of 20 pg/mL.

Pulmonary function was assessed by peak flow, forced vital capacity, and forced expiratory volume in first second using a spirometer (Micro spirometer; Micromedical, Rochester, England) before surgery and daily until discharge and 10 and 30 days after surgery.

Pain was assessed by a visual analog scale[26] at rest, during coughing, during mobilization before surgery, daily for 10 days after surgery, and again at 30 days after surgery. Fatigue was determined by a visual analog scale[27] before surgery, daily for 10 days after surgery, and 30 days after surgery. A self-care score,[28] including daily scoring of food intake, bowel and bladder function, washing, mobility, and mental needs, was recorded before surgery and daily after surgery until hospital discharge. Patients were discharged from the hospital according to the usual routine of the department: when they had passed stool and were physically and psychologically healthy.

Wounds were inspected daily until hospital discharge and at day 10 and 30 after surgery, and signs of infection or wound dehiscence were noted. Complications and reasons for exclusion were recorded.

For statistical calculations, the Mann-Whitney *U*, Fisher exact, and Friedman tests were used when appropriate. For evaluation of intraoperative respiratory and hemodynamic variables, means were calculated during the first hour after skin incision for each patient. Medians (50%) and 84% and 16% percentiles of these means, corresponding to mean ± SD of parametric statistics, were calculated for each group. All other values are given as medians (ranges). The Friedman test was used to evaluate and compare the overall response with time in all other variables. $P < .05$ was considered significant.

study (9 in the GL group and 8 in the CO_2 group). However, intraoperative hemodynamic and respiratory data of excluded patients were included in the results until surgery was converted. **Table 1** shows that patients were comparable regarding clinical parameters. There were significantly more women in the GL group ($P = .05$).

HEMODYNAMIC FACTORS AND RESPIRATORY FUNCTION DURING SURGERY

Significant differences between the groups were found only concerning descending aorta blood flow after 30 minutes ($P = .034$) and heart rate after 150 minutes ($P = .009$),

Table 1. Comparison of Clinical Data and Complications in 17 Patients Undergoing Laparoscopic Colonic Surgery*

	Group	
	Carbon Dioxide	Gasless
Sex ratio (male:female)	4:5	2:6
Age, y	75 (61-88)	76 (43-84)
Duration of surgery, min	150 (90-320)	145 (90-210)
Length of hospitalization, d	14 (5-46)	8 (6-16)
Blood loss, mL	0 (0-800)	50 (0-400)
Blood transfusions, No.	0 (0-4)	0 (0-3)

*Data are shown as medians (range) unless otherwise indicated.

in which the CO_2 group had a higher blood flow and a higher heart rate (**Figure 1**). Significantly higher values of $ETCO_2$ were found 30, 60, and 90 minutes after skin incision in the CO_2 group ($P = .009$, .007, and .04, respectively).

Calculating means across the first hour after skin incision revealed significantly higher central venous pressures ($P = .05$), $PaCO_2$ ($P = .03$), inspiration pressures ($P = .04$) and $ETCO_2$ tensions ($P = .01$) in the CO_2 group.

There were no differences in mean arterial pressure, thoracic impedance, central venous oxygen saturation, arterial and venous blood gasses, or inspirational pressure between the groups (**Table 2** and **Table 3**). Arterial pH decreased in both groups during surgery ($P = .008$) (Table 3). Temperature decreased during surgery in both groups ($P = .009$), but this decrease was moderate (median, <1°C) (Table 2).

PAIN

Patients in the CO_2 group had less pain during mobilization and coughing after surgery ($P = .008$ and .006, respectively) (**Figure 2**). No other intergroup differences were observed.

PULMONARY FUNCTION

Peak flow, forced vital capacity, and forced expiratory volume in 1 second decreased in both groups ($P = .001$). No intergroup differences were observed (**Figure 3**).

CONVALESCENCE

Fatigue increased in both groups ($P = .009$ in the GL group and .007 in the CO_2 group), and was more pronounced in the CO_2 group ($P = .04$). Self-care was normal on day 4 after surgery in the CO_2 group and on day 6 in the GL group. No intergroup differences were observed (**Figure 4**). Appetite was equal in both groups.

IL-6, CRP, AND PLASMINOGEN ACTIVATOR INHIBITOR-1

Plasma IL-6 levels increased significantly in both groups ($P = .007$). Serum CRP level increased significantly in both groups according to this ($P = .007$) (**Figure 5**). Plasminogen activator inhibitor-1 increased in both groups ($P = .05$) after surgery. No intergroup differences were observed in any variable.

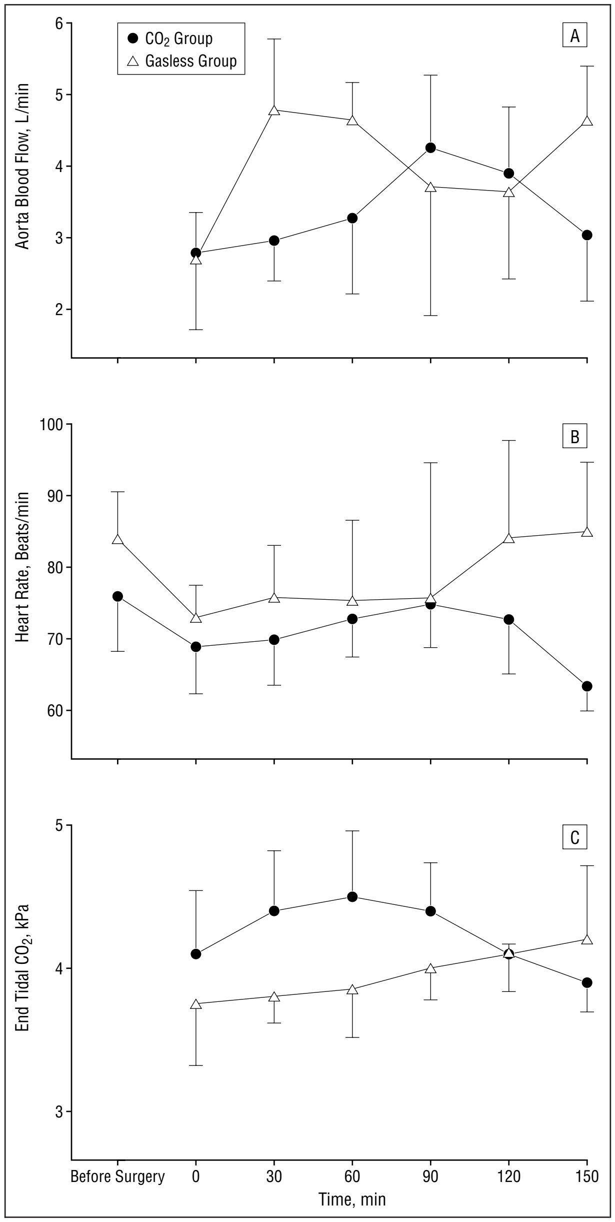

Figure 1. *Aorta blood flow, heart rate, and end-tidal carbon dioxide (CO_2) level in 17 patients undergoing colonic surgery. Results are presented as medians.*

HOLTER MONITORING

Two patients in the GL group had significant STdepression (>0.1 mV) during surgery for 1 to 2 hours, but with no clinical implications; 1 had a well-known but medically compensated cardiac disease, the other developed 2% ventricular extrasystoles after conversion to open surgery. Two patients in the CO_2 group had short episodes of ST depression during surgery lasting a few minutes, and another had 6% ventricular extrasystoles throughout Holter monitoring, but without any changes in fre-

Table 2. Perioperative Hemodynamic Factors*

Group	Percentile	CVP, cm H_2O	MAP, mm Hg	SvO_2, %	Thoracic Impedance, Ω	Temperature, °C Start	End
Carbon dioxide	16	13.5	73	77.8	43.0	35.6	35.0
	50	22.7	77	82.0	59.3	36.3	35.5
	84	27.5	88	88.1	71.0	36.9	35.8
Gasless	16	8.8	68	72.4	41.4	35.4	34.3
	50	13.8	75	82.0	45.4	36.0	35.2
	84	19.4	82	87.0	68.7	37.3	35.9
P	. . .	.04†	.19	.97	.54	.94	.76

**The means of the central venous pressure (CVP), mean arterial pressure (MAP), ventral venous oxygen saturation (SvO_2), thoracic impedance, and temperature were calculated for each patient during the first hour after incision. Ellipsis indicates data not applicable.*
†A significant difference between groups.

Table 3. Perioperative Respiratory Profile*

Group	Percentile	pH	$Paco_2$, kPa	Pao_2, kPa	Sao_2, %	SBE, mmol	HCO_3, mmol/L	P-Insp, cm H_2O
Carbon dioxide	16	7.31	5.17	18.5	97.5	−3.5	22.5	19
	50	7.37	5.50	22.1	98.3	−1.7	23.3	20
	84	7.40	6.15	30.8	99.0	−0.8	23.9	24
Gasless	16	7.34	4.65	13.1	96.0	−3.1	22.6	12
	50	7.39	5.00	27.1	98.3	−0.6	24.3	15
	84	7.46	5.61	29.1	99.0	0.3	26.1	20
P	. . .	.25	.03†	.80	.82	.28	.44	.04†

**Means of arterial pH, tension of carbon dioxide ($Paco_2$), tension of oxygen (Pao_2), saturation of oxygen (Sao_2), standard base excess (SBE), standard bicarbonate (HCO_3), and inspiratory pressure (P-insp) were calculated for each patient during the first hour after incision. Ellipsis indicates data not applicable.*
†A significant difference between groups.

quency during surgery. No significant intergroup differences were observed.

COMPLICATIONS

Three patients in the CO_2 group developed complications: 1 case of pneumonia, 1 case embolism of the right brachial artery, and 1 case of incarcerated inguinal hernia 4 days after colonic resection. No complications were observed in the GL group.

COMMENT

No important differences in intraoperative hemodynamic factors and postoperative convalescence, immunocompetence, or pulmonary function were observed in this study between patients undergoing GL vs CO_2 laparoscopy for colonic disease.

As expected, significantly higher values of central venous pressure, $Paco_2$, and inspiration pressure were found with CO_2 laparoscopy, reflecting increased intrathoracic pressure. These findings agree with previous reports.[16-18,29,30] We also observed higher arterial and $ETco_2$ levels in our patients during CO_2 laparoscopy in accordance with previous reports,[29] although no clinically important differences in outcome were observed between the groups.

Concerning cardiac output, flow measured in the descending aorta is lower than in the ascending aorta, but relative flow changes in the descending aorta correlate with relative changes of cardiac output.[31-33] Central venous oxygen saturation and thoracic impedance may also be used as an index of cardiac output.[22,34] We did not observe important differences in any parameter indirectly assessing changes in cardiac output (aorta blood flow, impedance, or central venous oxygen saturation). In accordance with our results, Marathe et al[35] observed a decrease in cardiac output only when intra-abdominal pressure was greater than 15 mm Hg in dogs; the usual 10 to 12 mm Hg for pneumoperitoneum seemed to be of minor importance, if any. In another experimental study,[36] hemodynamics were not affected at all during GL laparoscopy, whereas following CO_2-laparoscopy (15 mm Hg), significant hemodynamic changes were observed but cardiac output was unaffected. In contrast, others[4,6] have reported that an intra-abdominal pressure of 15 mm Hg may be associated with a 25% decrease in cardiac output.

Although hemodynamic factors were most stable during GL compared with conventional laparoscopic gynecological surgery, Johnson and Sibert[37] did not observe any clinically significant differences in their patients and concluded that GL laparoscopy was more technically difficult to perform. Use of low intra-abdominal pressure would probably benefit patients with decreased cardiopulmonary reserve.[30,38,39] In conclusion, GL laparoscopy causes less deterioration in intraoperative hemodynamic and respiratory parameters compared with CO_2 laparoscopy, but our results confirm that this is without clinical importance, as illustrated by the increasing metabolic acidosis in both groups. However, GL laparoscopy may benefit patients

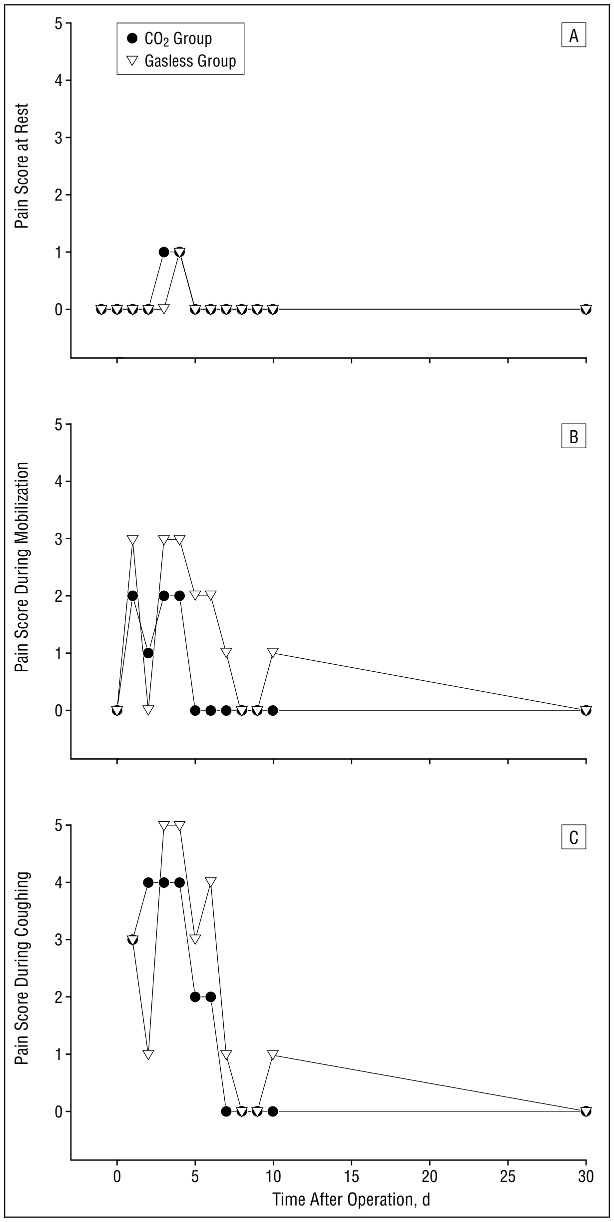

Figure 2. *Pain score (Visual Analog Scale) at rest, during mobilization, and during coughing in 17 patients undergoing laparoscopic colonic surgery. Results presented as medians. Patients in the carbon dioxide (CO_2) group had less pain during mobilization and coughing (*P *= .008 and .006, respectively).*

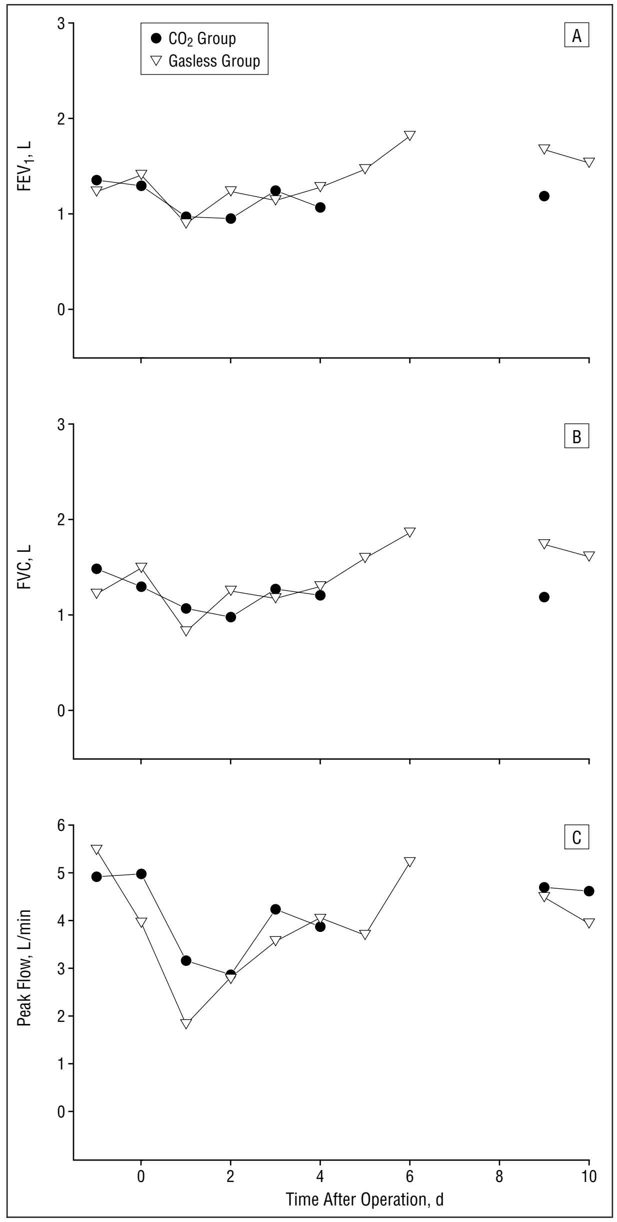

Figure 3. *Changes in forced expiratory volume in first second (FEV_1), forced vital capacity (FVC), and peak flow in 17 patients undergoing laparoscopic colonic surgery. Results presented as medians. No intergroup differences were observed.*

with severe cardiopulmonary problems, which could develop serious complications during high-pressure CO_2 laparoscopy.[9] However other studies support that CO_2 laparoscopy is safe in patients with severe cardiac disease when appropriate hemodynamic monitoring and adequate intraoperative support of cardiac functions are secured.[11,40,41]

Only a few studies have considered changes in hormones and cytokines following GL laparoscopy,[20,42] but IL-6 level seems to increase more following GL surgery when compared with open surgery. In our study, no intergroup differences were observed, although there was a trend toward higher IL-6 level in the GL group, and the magnitude of response was in accordance with the literature.[20,42] We were not able to confirm our earlier observation of a pronounced increase in IL-6 in CO_2 laparoscopy for colonic disease.[1] The changes in CRP and IL-6 in the present study are thus in accordance with other results following laparoscopic surgery,[3,42] and seem to be of little or no clinical importance. The significant postoperative increase of PAI-1 in both groups indicates that laparoscopic colonic surgery may not reduce the surgically induced modulation of fibrinolytic activity.

Differences in postoperative pain, use of analgesics, time of discharge from hospital, and other convalescence parameters have only been addressed in a few studies following GL laparoscopy.[29,43] In our randomized study, no significant differences in postoperative pain, pulmonary function, or any convalescence parameters

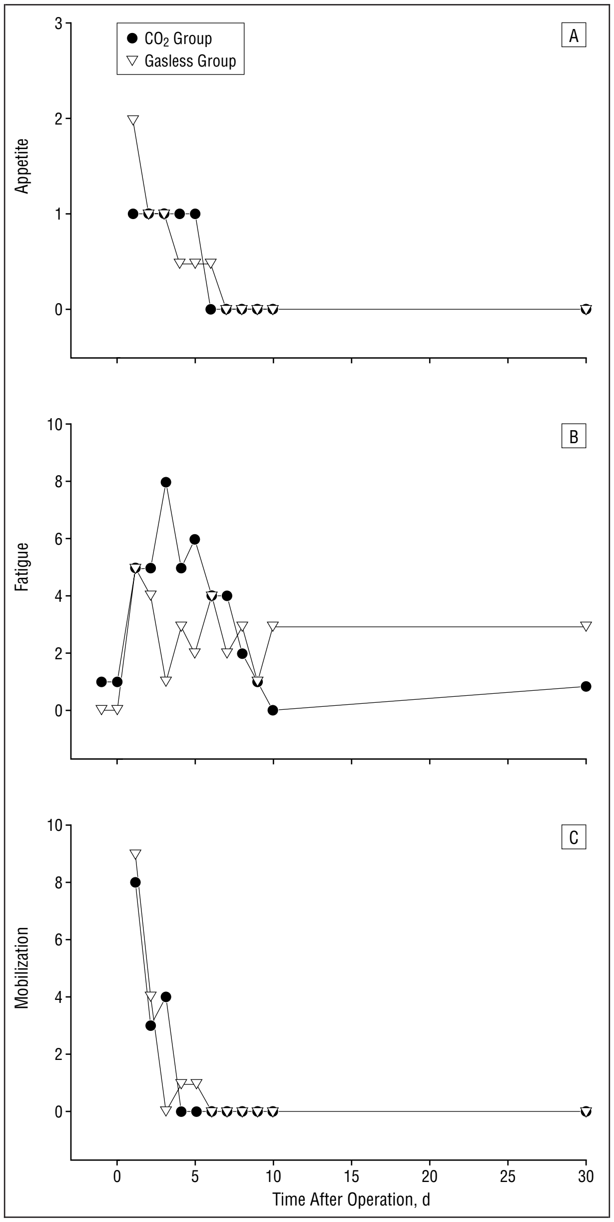

Figure 4. *Changes in appetite, fatigue, and mobilization scores (Visual Analog Scale) in 17 patients undergoing laparoscopic colonic surgery. Results presented as medians. Fatigue increased in both groups (*P *= .009 in the GL group and .007 in the* CO_2 *group) and was more pronounced in the carbon dioxide (*CO_2*) group (*P *= .04).*

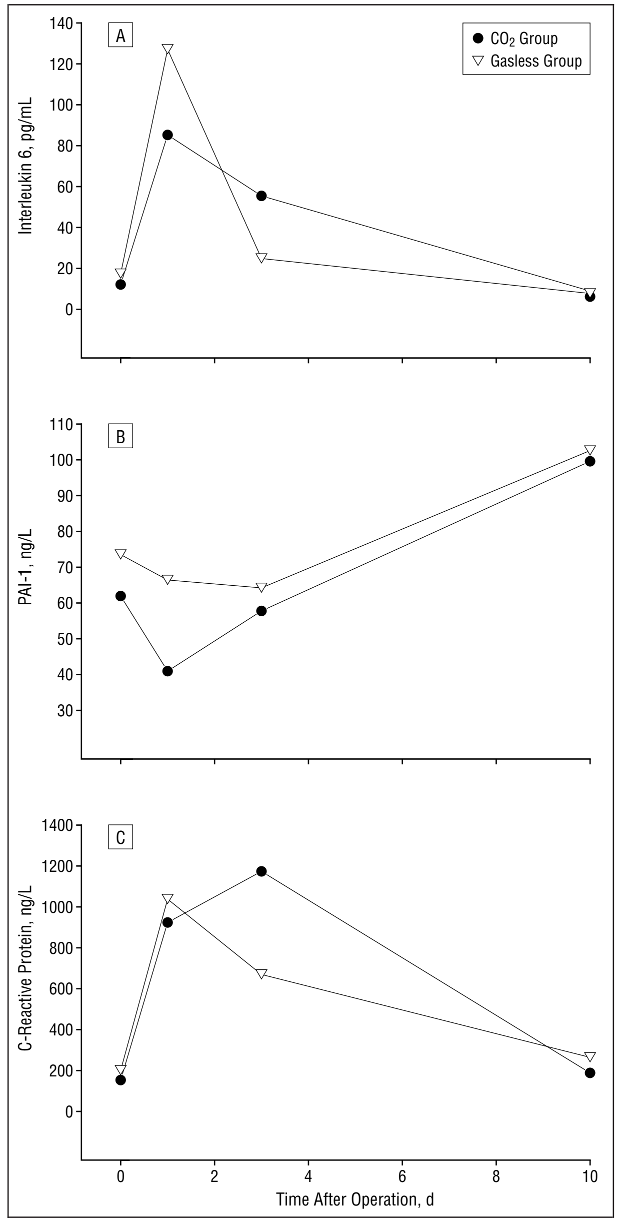

Figure 5. *Changes in interleukin 6, plasma plasminogen activator inhibitor type–1 (PAI-1), and C-reactive protein in 17 patients undergoing laparoscopic colonic surgery. Results presented as medians. No intergroup differences observed.*

were observed between the 2 groups, except for a small but clinically insignificant reduction in postoperative pain in CO_2 laparoscopy. These results agree with the other studies on GL vs CO_2 laparoscopic surgery.[29,43] The degree of impairment of pulmonary function in the present study was comparable to the results following open colonic surgery.[24,44] However, no conclusive data exist considering these parameters. Due to the small number of patients, our study does not allow any conclusion on the occurrence of complications, but we find the study sufficient to conclude that no clinically important differences considering convalescence between GL and CO_2 laparoscopy exist. It may be possible to find differences if the patients undergo optimized accelerated care regimens,[45] but this must be an issue for further clinical trials.

In conclusion, the results of this study suggest that colonic resection can be performed with both CO_2 and GL laparoscopy. However, the differences between the 2 methods are not marked, and GL laparoscopy does not seem to be more minimally invasive, especially considering the clinically important intraoperative hemodynamic and respiratory changes, as well as postoperative convalescence.

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