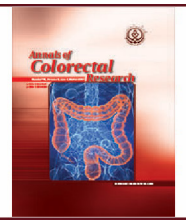
Original Article

Ann Colorectal Res 2020;8(2):79-87.



The Effect of Humidified, Warmed CO_2 during Open Colorectal Surgery on Body Temperature and Postoperative Pain: A Randomized Controlled Trial

Ju Yong Cheong*[1,2]*, MBBS, PHD, FRACS; *Anil Keshava*[1], MBBS, MS, FRACS; *Christopher John Young*[1], MBBS, MS, FRACS

[1]*Department of Colorectal Surgical, Concord Repatriation General Hospital, Sydney, Australia*
[2]*Discipline of Pathology, Charles Perkins Centre, Sydney Medical School, The University of Sydney, Sydney, Australia*

Corresponding authors:
Ju Yong Cheong, MBBS, PHD, FRACS;
Concord Institute of Academic Surgery, Department Colorectal Surgical, Concord Repatriation General Hospital, Teaching Hospital of University of Sydney, The University of Sydney. Sydney Medical School, Hospital Road, Concord, NSW 2139, Australia. Tel: +61 2 409 110 219; **Email:** Juyong.cheong@gmail.com

Received: 08-03-2020
Revised: 22-04-2020
Accepted: 22-04-2020

Abstract

Background: Open abdominal surgery exposes the intestine to negative ventilation (20 °C; 0-5% RH), which given the large surface area of the peritoneum, can facilitate the loss of body heat. This study examined whether warmed, humidified CO_2 (WHCO2) can reduce heat loss and decrease postoperative pain.
Methods: A randomized controlled trial was performed at a tertiary colorectal unit (Concord Repatriation General Hospital, The University of Sydney, Australia). The study group received WHCO2 at a rate of 10L/min. The control group did not receive any insufflation during the operation. Patients were over 18 years of age undergoing elective open colorectal operations. Core body temperature measurements were made every 15 minutes with a trans-esophageal probe. Postoperative pain was assessed via (1) the duration of use of patient-controlled analgesia (PCA) and (2) the total oral morphine equivalent daily dose (oral MEDD).
Results: In total, 39 patients were recruited in the study, with 20 receiving WHCO2. There was no difference in the core body temperature between the WHCO2 and control groups (36.1 vs. 35.9 °C; P=0.35). There was also no remarkable dissimilarity in the percentage of the operating time when the core body temperature dropped below the lower limit of normal, namely 35.8 °C (28.4 vs. 35.8 %; P=0.51), or fell below the level of hypothermia, i.e., 35°C (7.7 vs. 13.4 %; P=0.50). No differences in postoperative PCA duration and MEDD were noted between the WHCO2 and control groups.
Conclusion: We conclude that WHCO2 neither affected the core body temperature during open colorectal surgery nor the postoperative pain experienced.

Keywords: Humidified, warmed carbon dioxide. Pneumoperitoneum, Core body temperature, Postoperative pain, Colorectal surgery

Please cite this paper as:
Cheong JY, Keshava A, Young CJ. The Effect of Humidified, Warmed CO_2 during Open Colorectal Surgery on Body Temperature and Postoperative Pain: A Randomized Controlled Trial. *Ann Colorectal Res*. 2020;8(2):79-87. doi: 10.30476/ACRR.2020.46746.

Introduction

One of the problems of the open abdominal colorectal surgery is the exposure of the abdominal cavity to the ambient air. The setup of the operating room, where the air from the roof is blown down and out through the walls via negative ventilation, along with the dry, cold temperature of

the ambient air (20 °C; 0-5% relative humidity) leads to the continuous exposure of peritoneum to dry, cool air, leading to peritoneal/serosal desiccation (1). Peritoneal desiccation can lead to peritoneal inflammation, loss of barrier function, infection, and adhesion formation (1-4).

One pathway for mitigating bowel desiccation is the use of humidified, warmed carbon dioxide gas ($CO_{2(g)}$); $CO_{2(g)}$ is heavier (44 g/mole) and denser (1.97 kg/m^3) than the other components of atmospheric air at standard temperature and pressure (5). Insufflated $CO_{2(g)}$, therefore, tends to sink to the base of the abdominal wound. Furthermore, $CO_{2(g)}$ also assists in maintaining heat by creating a localized greenhouse effect within the abdominal cavity and is readily saturated to 100% with sterile-water, thereby acting to inhibit bowel desiccation (1, 2, 4, 6, 7).

In our previous systematic review of human laparoscopic studies and animal-based laparotomy insufflation, we found that studies have indicated that core body temperature is significantly lowered with exposure of peritoneum to ambient atmospheric conditions or to cold, dry pneumoperitoneum during laparoscopy (8). Our review also found that in human laparoscopic surgeries, of the 16 studies examined, only four showed a significant reduction in postoperative pain with the use of warmed, humidified carbon dioxide (WHCO2) (8). As yet, no human-based randomized controlled trials have examined the clinical effect of WHCO2 on postoperative pain, intraoperative temperature, and postoperative outcomes in patients undergoing open colorectal surgery.

This study aimed to determine for the first time in humans whether or not the use of WHCO2 during open colorectal surgery leads to better intraoperative control of core body temperature and decreased postoperative pain.

Methods

A randomized controlled trial based at a tertiary colorectal unit in Sydney, Australia (Concord Repatriation General Hospital, The University of Sydney) was performed on patients undergoing open colorectal surgery. The intervention group received warmed, humidified (37°C, 98%, RH) $CO_{2(g)}$ (WHCO2), while the control group had open colorectal surgery without any insufflation into the abdominal cavity.

Patients recruited were over 18 years of age and scheduled for elective open colorectal operations. Surgical indications included: curative colorectal carcinoma, polyposis syndromes, diverticular disease, rectal prolapse, and inflammatory bowel disease. Patients were excluded if they underwent emergency surgery, laparoscopic surgery, or suffered from poor lung function (oxygen use at home; $CO_{2(g)}$ retention; FEV_1 < 1L; FEV_1/FVC < 50%).

The HUMIGARD™ device (Fisher & Paykel Healthcare Ltd, Auckland, New Zealand) was used to deliver WHCO2, with the gas diffuser positioned at the upper end of the laparotomy wound at a depth of approximately 4 cm from the skin after the wound retractors were placed. The WHCO2 was delivered continuously at a rate of 10 L/min and a pressure of 4.5 bar until the laparotomy was closed.

Sample size calculation was performed using a measure of oxidative stress (3-chlorotyrosine), where it was hypothesized that the oxidative stress on the peritoneum results from peritoneal desiccation. The results of this peritoneal damage will be presented in another separate publication. For a power of 80%, at 5% significance, the sample size required was 40 patients. Data were analyzed using IBM SPSS version 23 (New York, USA) and GraphPad Prism version 7.0 (GraphPad Software Inc, California, USA). Continuous variables were tested using the D'Agostino-Pearson test. Groups were compared using the t-test/two-way analysis of variance (ANOVA) with Tukey's multiple comparisons test for continuous, parametric variables and the Mann-Whitney U test for continuous, non-parametric variables. The level of significance for all tests was set at $P<0.05$.

The examined outcome of interest was intraoperative core body temperature as well as postoperative pain. Core body temperature was measured every 15 min throughout the operation using a trans-esophageal probe. Postoperative pain was assessed via two methods: (1) duration of use of patient-controlled analgesia (PCA); (2) total oral morphine equivalent daily dose (oral MEDD). During the study, a new technique for measuring the intra-abdominal temperature was adopted. In addition to measuring the core body temperature every 15 minutes with the esophageal probe, a thermal FLIR E4 camera (FLIR systems, Oregon) was also used to measure intra-abdominal temperature. This electronic device had been pre-calibrated by the manufacturer. Unfortunately, as the study was already underway by the time the approval for its use was obtained from the Human Research Ethics Committee, the thermal imaging was only used for patients 32 to 40. Pictures were taken at 1 h from the start of the operation from 1 m vertically above the abdominal cavity.

Ethics approval was obtained (Sydney Local Health District Ethics Committee), and the trial was registered in ClinicalTrials.org (NCT02975947). All patients were seen pre-operatively by an investigator (Dr. JY Cheong), and the trial rationale and procedure were explained. Patients were then given an 'opt-in' participant information sheet, after which written informed consent was obtained before final enrolment and randomization to the various arms of the trial. Patients were randomized to the intervention and control arms by a random sequence generated using an online tool available at the www.random.org website. Patient allocation to specific groups was concealed in opaque numbered envelopes and kept in a central location and opened at the time of surgery

to reveal the assignment of patients to each group; both the patient and the investigator were blinded to the assignment.

Results

Initially, 40 patients were randomized into the two groups. From the recruited subjects, patient number 20 withdrew from the study after providing consent. The night before the scheduled operation, the patient was admitted and treated for acute pulmonary embolism requiring anticoagulation with intravenous heparin. Under these circumstances, the patient's operation was postponed, and the patient was hence withdrawn from the study. A CONSORT Flow Diagram outlining the small-scale clinical trial is presented in Figure 1.

Patient Demographics (Table 1)

Of the 39 patients recruited, 15 (37.5%) were female. There were seven female patients in the control group (36.8%) and eight in the WHCO2 group (40%). The mean age of the patients was 60.9 years (range: 32 to 87 years). The mean age of patients in the control group was 60.4 years, while that of the WHCO2 group was 61.3 years. The mean body mass index (BMI) was 26.5 (range: 14.1–43.1). The mean BMI of the control group was 27.7, whereas the mean BMI of the CO_2 treatment group was 25.3. Seventeen patients had undergone previous abdominal operations (43.5%), among which eight were in the control group (42.1%) and nine were in the $WHCO_{2(g)}$ group (45%). The mean estimated glomerular filtration rate (eGFR) was 73.36 mL/min/1.73 m^2 (95% CI: 63.76-82.97), with 42.1% of the patients determined to exhibit normal eGFR, while 36.8% presented with stage 2, 15.8% stage 3, and 5.3% exhibited stage 4 renal impairment. There was no statistically significant difference in the preoperative eGFR value between the CO_2 treatment group and the control group (81.90 vs. 73.36; p = 0.124). A total of nine patients (23.1%) had diabetes mellitus (DM); four in the control group (20%) and five in the CO_2 treatment group (26.3%). In total, 17 patients (43.5%) had hypertension (systolic blood pressure > 140 mmHg), seven of which were in the control group (35%) and ten of which were included in the treatment group (52.6%). The median American Society of Anesthesiologists (ASA) score was three across both groups. In total, nine patients regularly used anti-coagulants before the operation, four of which were in the control group. In total, 23.1% of the patients (nine patients) were active

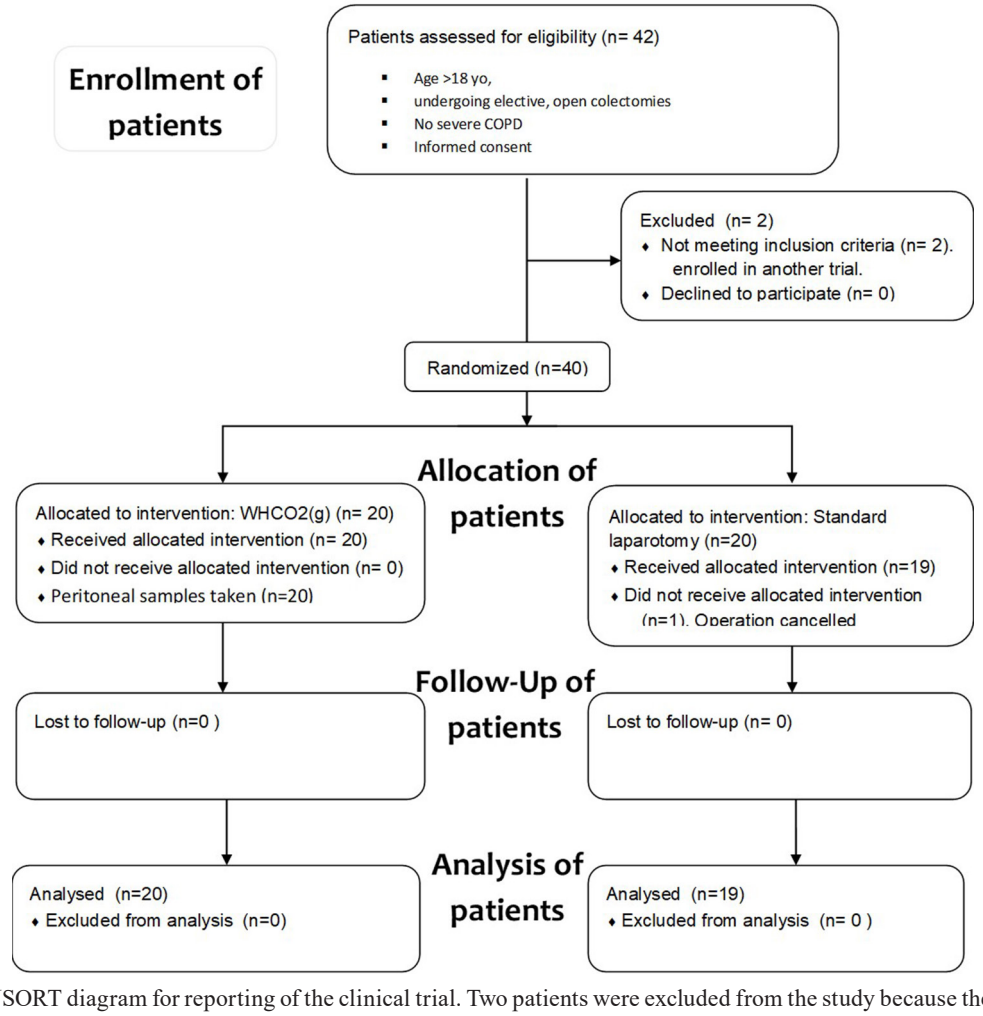


Figure 1: CONSORT diagram for reporting of the clinical trial. Two patients were excluded from the study because they were already enrolled in another study. One additional patient was excluded because of pulmonary embolism preventing the subject from having the planned abdominal surgery.

Table 1: Summary of patient demographics in the Control and CO_2 treatment groups[a]

Demographics	Control group (n = 19)	CO_2 treatment group (n = 20)	P value
Female	7 (36.8%)	8 (40%)	0.839
Age (years)	60.47	61.35	0.863
BMI (Mean)	27.71	25.36	0.334
BMI (overweight or obese)	10 (55.5%)	7 (36.8%)	0.13
IHD	2 (10%)	4 (21.0%)	0.339
COPD	0 (0%)	1 (5.2%)	0.299
EGFR(mL/min/1.73m^2)	73.36	81.9	0.124
Diabetes Mellitus	4 (20%)	5 (26.3%)	0.64
Hypertension	7 (35%)	10 (52.6%)	0.267
Any Comorbidities	8 (40%)	12 (63.1%)	0.148
Number of comorbidities (mean)	0.736	1.05	0.332
ASA score (mean)	2.52	2.6	0.753
Preoperative Haemoglobin level (g/dL)	130.68	125.05	0.485
Preoperative INR	1.04	1.08	0.562
Anticoagulants	4 (21.05%)	5 (25%)	0.770
Smoker	6 (31.6%)	3 (15%)	0.219
Mobility (4 flights of stairs)	14 (73.7%)	12 (60%)	0.365

a No significant difference noted between the CO_2 treatment and the Control groups with regards to all patient demographics, indicating adequate randomization process

smokers. In the control group, six patients (31.6%) were smokers, whereas in the CO_2 treatment group, three patients (15%) were smokers. Each patient's level of mobility was assessed preoperatively by asking the patient to walk up flights of stairs until they required a break. In total, 26 patients (66.6%) had the requisite mobility walk up four flights of stairs without stopping for a period of rest. In the control group, 14 patients (73.7%) were able to go up four flights of stairs; this number was 12 in the CO_2 treatment group (60%).

Operations Performed

The operations performed are presented in Table 2. In total, 45 open abdominal procedures were performed on the 39 randomized patients. One case of partial gastrectomy was recorded for a patient with long-term fistulizing Crohn's disease involving the anterior surface of the stomach.

The mean operative time was 288 min (95% CI: 241.5–335.7 min). The mean operative time for the control group was 284.05 min, with a 95% CI of 217.39–350 min. The mean operative time for the CO_2 treatment group was 292. 9 min, with a 95% CI of 220–365 min. There was no statistically significant difference in operative time between the two groups (P=0.85). In the CO_2 treatment group, the CO_2 gas was insufflated at a constant rate of 10 L/min. The mean duration of CO_2 insufflation amongst the 20 patients that received CO_2 treatment was 203.7 min (151.2–256.2 min).

Table 2: Operations performed in the 39 patients (both CO_2 treatment and control groups)

Operation performed	N
Abdominoperineal resection	4
Right hemicolectomy	6
Anterior resection (high)	1
Anterior resection (low)	5
Anterior resection (ultralow)	4
Pelvic exenteration	2
Repair parastomal hernia	4
Repair enterocutaneous fistula	3
Repair of Colon-to-another organ fistula	2
Reversal of end colostomy (Hartman's)	6
Reversal of ileostomy	3
Small bowel resection, adhesiolysis for IBD	2
Subtotal colectomy	2
Partial gastrectomy	1

Postoperative Outcome

The mean duration of hospital stay was 15.9 days (95% CI: 10.6-21.2 days). There was no statistically significant discrepancy in the mean duration of hospital stay between the CO_2 group and the control group (16.7 vs. 15.1 days; P=0.76). The definition of persistent ileus adopted from the literature was a failure of the patient to eat, pass flatus, or evacuate the bowel within five days after a laparotomy (9). Of the 39 patients, one patient (from the CO_2 treatment group) was excluded from analysis because they developed complications requiring multiple operations. Eleven out of the 38 remaining patients developed persistent ileus (28.9%). The rate of persistent ileus was much higher in the control group (42.1%) as compared with the CO_2 group (15.7%); however, this did not reach statistical significance (P=0.07). Nine of the combined total of 39 patients (23.1%) developed a postoperative wound infection. In the control group, six patients (31.6%) developed a postoperative wound infection, while in the CO_2 treatment group, three patients (15%) developed a postoperative wound infection; this was not statistically significant (P=0.22).

Of the 39 patients, nine patients were excluded because they did not have bowel anastomosis (five

in the CO_2 group, four in the control group). Amongst patients with bowel anastomosis, one patient (3.3%) developed an anastomotic leak (from the CO2 group).

The mean number of days until a subject passed stool postoperatively was 4.6 days (95% CI: 3.6–5.7 days), with a median of 3 days (interquartile range: 3.5 days). Defecation of stool tended to occur earlier in the CO_2 treatment group as compared with the control group; this had no statistical significance (3.7 vs. 5.5 days; P=0.09), although the *p*-value may suggest a weak trend.

Seven patients (17.9%) had an unexpected return to the operating theatre (OT); three (15%) in the CO_2 group and four (21.1%) in the control group. This was not statistically significant (P=0.62).

Seven patients were readmitted (17.9%) expectedly after discharge from the index admission. In the control group, three patients (15.8%) were readmitted, while in the CO_2 treatment group, four patients required readmission (20%). This weak difference was not statistically significant (P=0.73).

Postoperative Pain

Postoperative pain was assessed via two methods: (1) duration of use of patient-controlled analgesia (PCA) and (2) total oral morphine equivalent daily dose (oral MEDD).

In the analysis of the use of PCA, three patients were excluded. One patient (CO_2 group) did not have a PCA; two were excluded because they had postoperative complications requiring repeated operations and prolonged intubation.

The mean postoperative duration of PCA use was 3.4 days (95% CI: 2.8–3.97 days); the minimum duration was one day and the maximum was nine days (Figure 2-a). The mean duration of PCA use for the control group was 3.38 days (95% CI: 2.6–4.2 days) (Figure 2-b), and the mean duration in the CO_2 treatment group was 3.4 days (95% CI: 2.43–4.34 days) (Figure 2-c). There was no statistically significant difference in PCA use duration between the two groups (P=0.99).

In the oral MEDD calculation, six patients were excluded. One patient was excluded because they received epidural analgesia. One patient had prolonged intubation and stayed in the intensive care unit postoperatively. Two patients were excluded because of histories of chronic pain, requiring multiple analgesic medications even pre-operatively. Two patients were excluded due to incomplete documentation of analgesia requirements in their medication charts. Of the 39 patients, oral MEDD was calculated in 33 patients for which the mean MEDD requirement on each of the first four postoperative days is presented in Figure 3.

The mean oral MEDD score on day 1 was 202.6 (95% CI: 139.7–265.5), with a minimum of 22 and a maximum of 800. On day 2, the mean oral MEDD score was 104.0 (95% CI: 66.3–141.7). This value was 59.11 on day 3 (95% CI: 35.2 – 83.0) and 51.3 on day 4 (95% CI: 27.0–75.2).

The average oral MEDD was 104.3 (95% CI: 73.3–135.3). The oral MEDD scores of the CO_2 treatment and control groups are compared in Table 3. Between the two groups, there was no statistically significant difference in neither the oral MEDD score on the first four postoperative days nor the average MEDD requirement.

Core Body Temperature

Core body temperature was measured using a trans-

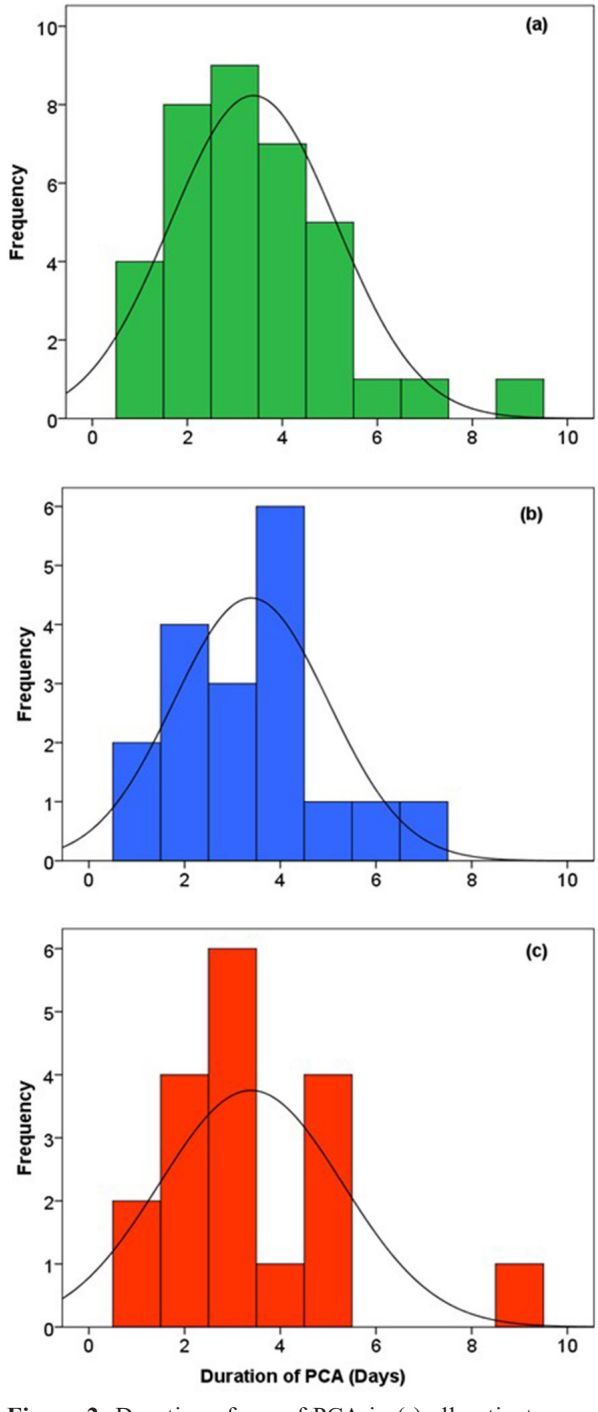


Figure 2: Duration of use of PCA in (a) all patients-green (b) control group-blue and (c) CO_2 treatment group-red. No statistically significant difference between CO_2 treatment and control group. Student's t-test for equality of means (p = 0.99) (IBM SPSS Statistics, v 23.0, New York, IBM Corporation).

esophageal probe with readings being taken every 15 min for all 39 patients. The graph in Figure 4 shows the individual temperatures of patients in the control and CO_2 treatment groups. The minimum temperature for the control group was 33 °C, whereas the minimum temperature for the CO_2 treatment group was 34.1°C.

The mean core body temperature throughout the operation was compared between the CO_2 and control groups, the results of which are presented in Figure 5. The mean core body temperature was 35.9 °C in the control group and 36.1°C in the CO_2 group; there was no statistically significant difference between the two groups (P=0.35).

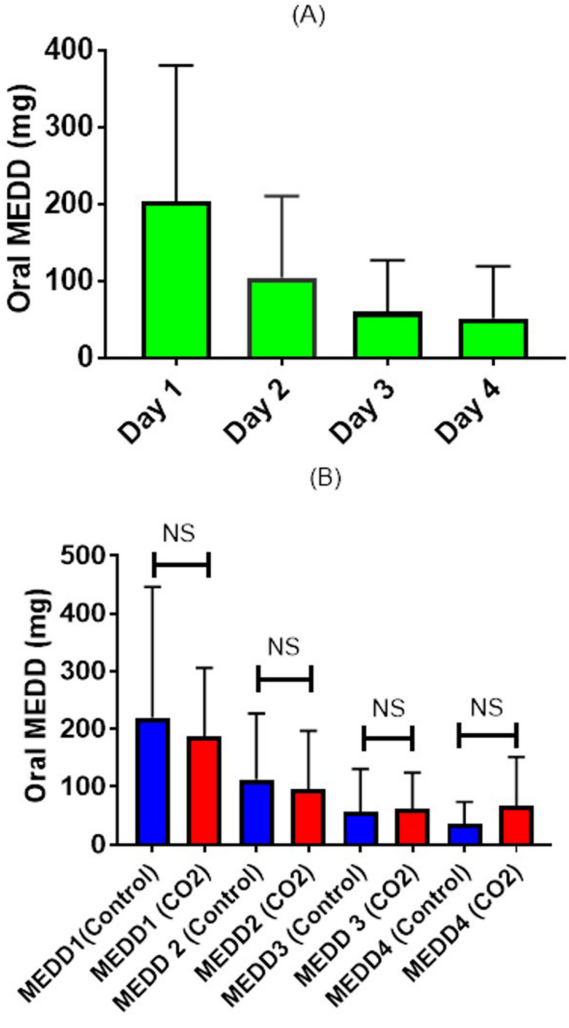


Figure 3: Oral MEDD requirement on postoperative days 1-4 in the (A) combined cohort, (B) control and CO_2 treatment groups. Histogram showing mean + SD; NS-non significant. No significant difference in oral MEDD between CO_2 and control groups. Graph created with GraphPad-Prism for windows, v.7.00, California, USA.

Temperature Dipping Below 35.8°C

The normal body temperature is 35.8 to 37.4 °C. Throughout the operation, the patient's core body temperature was monitored continuously, and patients were actively warmed using modalities including BairHuggers™ (3M Company, Minnesota) and fluid warmers. The percentage of time that the core body temperature readings performed at 15-minute intervals dipped below the level of 35.8°C was compared between the control and the CO_2 treatment groups. In the control group, core temperature dipped below 35.8 °C in 36.1% of the operational duration; this was lower (28.4%) in the CO_2 group but did the difference did not reach statistical significance (P=0.51).

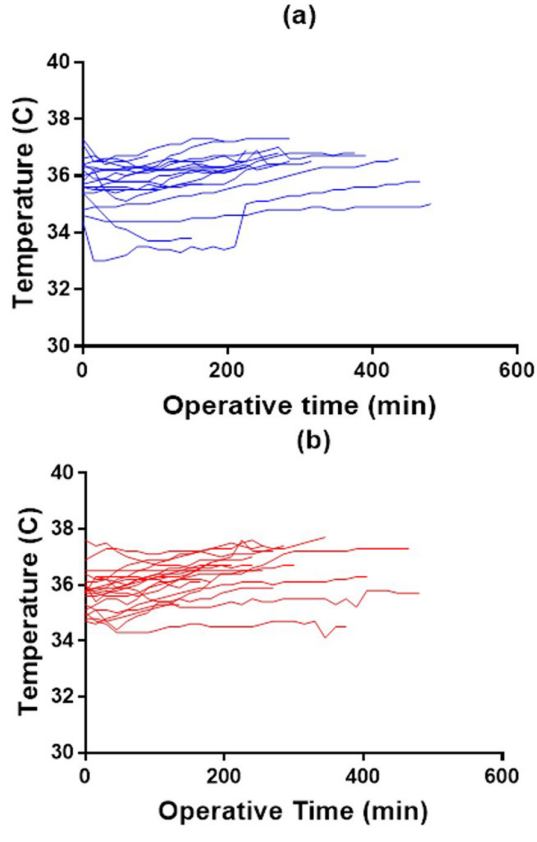


Figure 4: Core body temperature in (a) control and (b) CO_2 treatment groups. Each line represents an individual patient's temperature readings throughout the operation. Graph created with GraphPad-Prism for windows, v.7.00, California, USA.

Table 3: Oral MEDD requirement in the Control and CO_2 treatment groups on day 1, day 2, day 3, day 4[a]

Oral MEDD SCORE	The control group (16)	CO_2 group (17)	P value
Day1	219.1938	187.0341	0.61
Day2	112.4538	96.0635	0.665
Day3	56.05	62.0047	0.804
Day4	35.0688	66.6176	0.183
Average	105.6916	102.93	0.929
PCA use (days)	3.38	3.38	0.99

[a] No statistically significant difference was detected between two groups with regards to oMEDD and duration of PCA use. Statistics calculated using Student's t-test for equality of means. (IBM SPSS Statistics, v 23.0, New York, IBM Corporation)

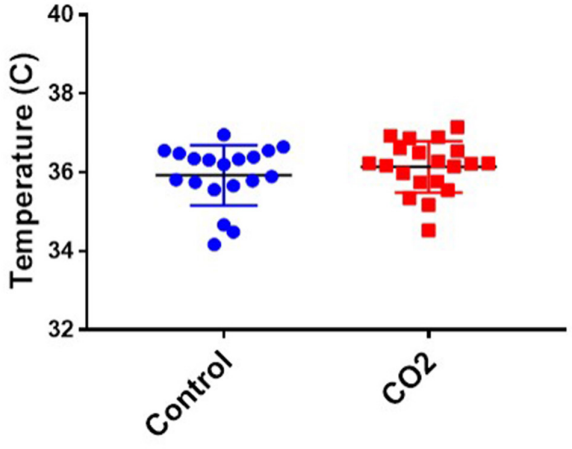


Figure 5: Mean of the core body temperatures in the CO_2 treatment group and control group of patients (blue=control group; red=CO_2 treatment group). No statistically significant difference between CO_2 and control groups. Student's t-test for equality of means (p = 0.35). Graph created with GraphPad-Prism for windows, v.7.00, California, USA.

Temperature Dipping Below 35 °C (Hypothermia)

Hypothermia is defined as an involuntary drop in core body temperature to below 35.0 °C. The percentage of the duration of operating time where the core body temperature dropped below 35.0 °C was evaluated. In the control group, the core body temperature dropped below 35.0 °C in 13.4% of the duration of the operation, whereas in the CO_2 treatment group, only in 7.7% of the operative duration did the core body temperature reach the level of hypothermia, although again this was not statistically significant (P=0.50).

Intra-Abdominal Temperature

For nine patients (patients 32–40), intra-abdominal thermal images were taken throughout the operation, including four patients in the control group and five in the CO_2 treatment group. Representative images of the intra-abdominal temperatures in the control and CO_2 treatment groups are presented in Figure 6.

Using the software FLIRTOOLS™ (FLIR systems, Oregon), temperature readings were taken from a series of points on the thermal images. At one hour into the operation, the mean intra-abdominal temperature was 29.9 °C in the control group and 34.4°C in the CO_2 treatment group. No statistical test was done as the number of patients was small and only a single time point was used.

Correlation Analysis

The core body temperature was compared between groups that developed and did not develop ileus. In the eleven patients who developed ileus, the mean core body temperature was 35.8 °C, whereas among the 27 patients who did not develop ileus, the mean core body temperature during the operation was 36.17 °C. This difference was not, however, statistically significant (P=0.18).

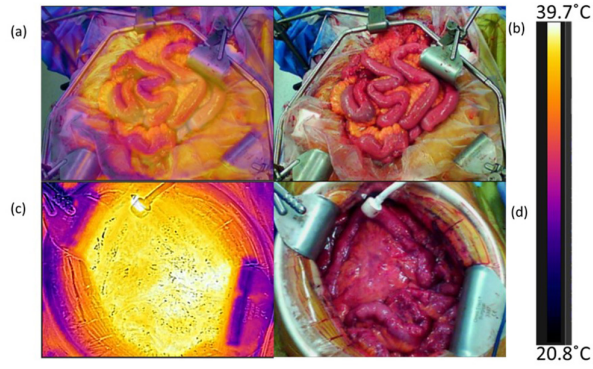


Figure 6: Images show thermal and corresponding intra-abdominal images for the control (a-b) and warm, humidified CO_2 treatment (c-d) groups, respectively.

There was a weak but significant negative correlation between age and intraoperative core body temperature (Pearson's correlation coefficient r: -0.532; P<0.001). This would mean that the older the patients were, the lower their core body temperature during the operation.

There was a negative correlation between BMI and the core body temperature during the operation (Pearson's correlation coefficient r: -0.390; P=0.014). This meant the more obese the patient, the lower the core body temperature during the operation. One possible explanation may be that the more obese the patient, the larger the surface area for heat loss during the operation.

Discussion

In our study, no divergence in core body temperature was detected between the WHCO2 and control groups. There was also no difference in the rate of hypothermia throughout the operation between the two groups. To date, this is the only human-based study that has examined the effect of CO2 on core body temperature during open abdominal operations. The literature on the effect of WHCO2 in laparoscopic studies is divided: seven human studies found significantly higher core body temperatures in the treatment (humidified, warmed CO_2) group than the control (cold, dry CO_2), whereas nine studies did not find any significant difference (10-18). The largest human-based RCT involved 195 patients undergoing laparoscopic appendectomy (15), which revealed no considerable difference in core body temperature between the treatment group and the control group. However, the next-largest human RCT, based on 148 patients undergoing laparoscopic cholecystectomy, found higher core temperatures in the WHCO2 group relative to the control (37.07 °C vs. 36.85 °C; P=0.01) (19). Another study found that the core temperature decreased in both the treatment and control groups; however, the extent of decrease in temperature was greater in the treatment group than in the control (*c.f.*, control: 0.7 °C and CO_2 group: 0.3 °C; P=0.01) (20). In that study, in the treatment group, the CO_2

was heated to 37 °C but not humidified. Thus, it appears that WHCO2 has no effect on the core body temperature during open abdominal surgery. This may be due to the confounding effect of active warming every patient receives during an operation. An interesting finding of ours was that the intra-abdominal temperature was markedly lower in the control group as compared with the WHCO2 group; however, no statistical analysis was performed due to the small number analyzed.

This study also found no difference in postoperative pain experienced between the WHCO2 and control groups, with no differences in the duration of PCA and MEDD requirements. The evidence in the literature on the effect of WHCO2 during laparoscopic surgeries has also been conflicting. Nine studies (with a total of 602 patients) found no difference in postoperative pain (10, 12, 15, 17, 18, 21-24), whereas seven studies (with a combined total of 621 patients) found that pain was significantly lowered with the use of WHCO2 (13, 14, 19, 25-28).

Our study discovered no clinical difference between the WHCO2 and control groups with regard to postoperative outcomes; it would appear the WHCO2 does not confer any clinical benefit. However, while not attaining statistical significance, the rate of ileus was lower and the return of bowel function was quicker in the WHCO2 group. This may indicate that the study was underpowered to detect a meaningful clinical difference.

A subsequent study should be designed to detect significant clinical outcomes. Based upon our results, a power calculation based on the prolonged ileus rate of 42.1% vs. 15.7%, with α of 0.05, and power of 80% revealed the number need for the trial to be 90, with 45 patients in each of the CO2 and control groups. We would also recommend all patients have intra-abdominal temperatures measured along with core body temperatures.

Conclusion

Warmed, humidified CO2 confers no benefit with regard to the maintenance of core body temperature during open colorectal surgery and the postoperative pain experienced.

Acknowledgement

We would like to thank Victoria Cran, the colorectal nursing unit manager of Concord Repatriation General hospital.

Conflicts of interests: None declared.

References

1. M. Persson and J. van Der Linden, "Intraoperative CO2 insufflation can decrease the risk of surgical site infection," *Medical Hypothesis,* vol. 71, no. 1, pp. 8-13, 2008.
2. M. Binder, "Humidification during laparoscopic surgery: overview of the clinical benefits of using humidified gas during laparoscopic surgery.," *Archives of gynaecology and obstetrics,* vol. 292, no. 5, pp. 955-971, 2015.
3. M. Tsuchiya, E. Sato, M. Inoue and A. Asada, "Open abdominal surgery increases intraoperative oxidative stress: can it be prevented?," *Anesthesiae and analgesia,* vol. 107, no. 6, pp. 1946-1952, 2008.
4. J. van der Linden and M. Persson, "CO2 field flooding may also reduce oxidative stress in open surgery," *Anesthesiae and analgesia,* vol. 109, no. 2, pp. 683-684, 2009.
5. R. Publishing, "Reference: Is CO2 Heavier Than Air?," 2017. [Online]. Available: https://www.reference.com/science/co2-heavier-air-b69c3fe7a671fbad?qo=contentSimilarQuestions#. [Accessed 2017].
6. M. Persson, J. Flock and J. Van der Linden, "Antiseptic wound ventilation with a gas diffuser: a new intraoperative method to prevent surgical wound infection?," *Journal of Hospital infection,* vol. 54, no. 4, pp. 294-299, 2003.
7. M. Persson and J. van der Linden, "Wound ventilation with carbon dioxide: a simple method to prevent direct airborne contamination during cardiac surgery?," *Journal of Hospital Infection,* vol. 56, no. 2, pp. 131-136, 2004.
8. J. Cheong, A. Keshava, P. Witting and C. Young, "Effects of intraoperative warmed, humidified CO2 insufflation during abdominal surgery: a review.," *Annals of Coloproctology,* vol. 34, no. 3, p. 125–137, 2018.
9. S. Sajja and M. Schein, "Early postoperative small bowel obstruction," *British Journal of Surgery,* vol. 91, no. 6, pp. 683-691, 2004.
10. J. Champion and M. Williams, "Prospective randomized trial of heated humidified versus cold dry carbon dioxide insufflation during laparoscopic gastric bypass," *Surgery for Obesity and related diseases,* vol. 2, no. 4, pp. 445-449, 2006.
11. C. Yeh, S. Kwok, M. Chan and J. Tjandra, "Prospective, case-matched study of heated and humidified carbon dioxide insufflation in laparoscopic colorectal surgery," *Colorectal Disease,* vol. 9, no. 8, pp. 695-700, 2007.
12. S. Saad, I. Minor, T. Mohri and M. Nagelschmidt, "The clinical impact of warmed insufflation carbon dioxide gas for laparoscopic cholecystectomy," *Surgical Endoscopy,* vol. 14, no. 9, pp. 787-790, 2000.
13. W. Mouton, J. Bessell, S. Millard, P. Baxter and G. Maddern, "A randomized controlled trial assessing the benefit of humidified insufflation gas during laparoscopic surgery," *Surgical Endoscopy,* vol. 13, pp. 106-108, 1999.
14. Herrmann and R. De Wilde, "Insufflation with humidified and heated carbon dioxide in short-term laparoscopy: a double-blinded randomized controlled trial," *Biomed research international,* 2015.
15. T. Yu, J. Hamill, A. Liley and A. Hill, "Warm, humidified carbon dioxide gas insufflation for laparoscopic appendectomy in children: a double-blinded randomized controlled trial," *Annals of Surgery,* vol. 257, pp. 44-53, 2013.
16. Ozgonul, C. Erkan, G. Mehmet, B. Zeynep and U. Ali, "The effects of isothermic or hypothermic carbon dioxide pneumoperitoneum on

arterial blood gases," *Saudi Medical Journal,* vol. 28, no. 11, pp. 1662-1665, 2007.

17. J. Manwaring, E. Readman and P. Maher, "The effect of heated humidified carbon dioxide on postoperative pain, core temperature, and recovery times in patients having laparoscopic surgery: a randomized controlled trial," *Journal of minimally invasive gynecology,* vol. 15, no. 2, pp. 161-165, 2008.

18. S. Davis, D. Mikami, M. Newlin, B. Needleman, M. Barrett, R. Fries, T. Larson, J. Dundon, M. Goldblatt and W. Melvin, "Heating and humidifying of carbon dioxide during pneumoperitoneum is not indicated: a prospective randomized trial," *Surgical Endoscopy,* vol. 20, no. 1, pp. 153-158, 2006.

19. B. Klugsberger, M. Schreiner, A. Rothe, D. Haas, P. Oppelt and A. Shamiyeh, "Warmed, humidified carbon dioxide insufflation versus standard carbon dioxide in laparoscopic cholecystectomy: a double-blinded randomized controlled trial.," *Surgical Endoscopy,* vol. 28, no. 9, pp. 2656-2660, 2014.

20. K. Nelskylä, A. Yli-Hankala, J. Sjöberg, I. Korhonen and K. Korttila, "Warming of insufflation gas during laparoscopic hysterectomy: effect on body temperature and the autonomic nervous system," *Acta anaesthesiologica Scandinavica,* vol. 43, no. 10, pp. 974-978, 1999.

21. R. Savel, S. Balasubramanya, S. Lasheen, T. Gaprindashvili, E. Arabov, R. Fazylov, R. Lazzaro and J. Macura, "Beneficial effects of humidified, warmed carbon dioxide insufflation during laparoscopic bariatric surgery: a randomized clinical trial," *Obesity Surgery,* vol. 15, no. 1, pp. 64-69, 2005.

22. N. Nguyen, G. Furdui, N. Fleming, S. Lee, C. Goldman, A. Singh and B. Wolfe, "Effect of heated and humidified carbon dioxide gas on core temperature and postoperative pain: a randomized trial.," *Surgical Endoscopy,* vol. 16, no. 7, pp. 1050-1054, 2002.

23. D. Farley, S. Greenlee, D. Larson and J. Harrington, "Double-blind, prospective, randomized study of warmed, humidified carbon dioxide insufflation vs standard carbon dioxide for patients undergoing laparoscopic cholecystectomy," *Archives of surgery,* vol. 139, no. 7, pp. 739-743, 2004.

24. T. Sammour, A. Kahokehr, J. Hayes, M. Hulme-Moir and A. Hill, "Warming and humidification of insufflation carbon dioxide in laparoscopic colonic surgery: a double-blinded randomized controlled trial," *Annals of surgery,* vol. 251, no. 6, pp. 1024-1033, 2010.

25. M. Hamza, B. Schneider, P. White, A. Recart, L. Villegas, B. Ogunnaike, D. Provost and D. Jones, "Heated and humidified insufflation during laparoscopic gastric bypass surgery: effect on temperature, postoperative pain, and recovery outcomes," *Journal of laparoendoscopic & advanced surgical techniques. Part A. ,* vol. 15, no. 1, pp. 6-12, 2005.

26. T. Beste, J. Daucher and D. Holbert, "Humidified compared with dry, heated carbon dioxide at laparoscopy to reduce pain," *Obstetrics and Gynaecology,* vol. 107, no. 2, pp. 263-268, 2006.

27. S. Kissler, M. Haas, R. Strohmeier, H. Schmitt, A. Rody, M. Kaufmann and E. Siebzehnruebl, "Effect of humidified and heated CO2 during gynecologic laparoscopic surgery on analgesic requirements and postoperative pain," *The Journal of the American Association of Gynecologic Laparoscopists,* vol. 11, no. 4, pp. 473-477, 2004.

28. R. Benavides, A. Wong and H. Nguyen, "Improved outcomes for lap-banding using the insuflow device compared with heated-only gas," *Journal of the Society of Laparoendoscopic Surgeons,* vol. 13, no. 3, pp. 302-305, 2009.

29. D. Brown, H. Brugger, J. Boyd and P. Paal, "Accidental hypothermia," *New England Journal of Medicine,* vol. 367, pp. 1930-1938, 2012.

30. J. Horsley, "Peritonitis," *Archives of Surgery,* vol. 36, no. 2, pp. 190-224, 1938.

31. Y. Peng, M. Zheng, Q. Ye, X. Chen, B. Yu and B. Liu, "Heated and humidified CO2 prevents hypothermia, peritoneal injury, and intra-abdominal adhesions during prolonged laparoscopic insufflations," *Journal of Surgical Research,* vol. 151, no. 1, pp. 40-47, 2009.

32. E. Hazebroek, M. Schreve, P. Visser, R. De Bruin, R. Marquet and H. Bonjer, "Impact of temperature and humidity of carbon dioxide pneumoperitoneum on body temperature and peritoneal Morphology," *Journal of laparoendoscopic & advanced surgical techniques. Part A,* vol. 12, no. 5, pp. 355-364, 2002.

33. J. Bessell, A. Karatassas, J. Patterson, G. Jamieson and G. Maddern, "Hypothermia induced by laparoscopic insufflation. A randomized study in a pig model," *Surgical Endoscopy,* vol. 9, no. 7, pp. 791-796, 1995.

34. M. Bäcklund, I. Kellokumpu, T. Scheinin, K. von Smitten, I. Tikkanen and L. Lindgren, " Effect of temperature of insufflated CO2 during and after prolonged laparoscopic surgery," *Surgical Endoscopy ,* vol. 12, no. 9, pp. 1126-1130, 1998.

35. D. Ott, "Correction of laparoscopic insufflation hypothermia," *Journal of laparoendoscopic surgery,* vol. 1, no. 4, pp. 183-186, 1991.

36. World Health Organisation, "Adult: Body Mass Index (BMI) classification," 2017. [Online]. Available: http://www.who.int/mediacentre/factsheets/fs311/en/. [Accessed June 2017].

37. N. K. F. K. D. O. Q. I. (. KDOQI), "KDOQI Clinical Practice Guidelines for Chronic Kidney Disease: Evaluation, Classification, and Stratification," 2002. [Online]. Available: http://www2.kidney.org/professionals/kdoqi/guidelines_ckd/p4_class_g1.htm. [Accessed June 2017].

38. N. H. F. o. Australia., "Guidelines for the diagnosis and management of Hypertension in adults," 2016. [Online]. Available: https://www.heartfoundation.org.au/images/uploads/publications/PRO-167_Hypertension-guideline-2016_WEB.pdf. [Accessed 2017].

39. American Society of Anesthesiologist, "ASA Physical Status classification System," 2014. [Online]. Available: https://www.asahq.org/resources/clinical-information/asa-physical-status-classification-system. [Accessed 2014].

40. D. Baron, H. Hochrieser, M. Posch, B. Metnitz, A. Rhodes, R. Moreno, R. Pearse, P. Metnitz, E. S. O. S. (. g. f. T. G. o. E. S. o. I. C. Medicine and E. S. o. Anaesthesiology., "Preoperative anaemia is associated with poor clinical outcome in non-cardiac surgery patients," *British Journal of Anesthesia,* vol. 113, no. 3, pp. 416-423, 2014.

41. D. Dindo, N. Demartines and P. Clavien, "Classification of surgical complications- a new proposal with evaluation in a cohort of 6336 patients and results of a survey," *Annals of Surgery,* vol. 240, no. 2, pp. 205-213, 2004.