

Intraoperative Local Insufflation of Warmed Humidified CO₂ Increases Open Wound and Core Temperatures: A Randomized Clinical Trial

Joana M. K. Frey · Martin Janson ·
Monika Svanfeldt · Peter K. Svenarud ·
Jan A. van der Linden

Published online: 7 August 2012
© Société Internationale de Chirurgie 2012

Abstract

Background The open surgical wound is exposed to cold dry ambient air, resulting in substantial heat loss through radiation, evaporation, and convection. At the same time, anesthesia decreases the patient's core temperature. Despite preventive measures, mild intraoperative hypothermia has been associated with postoperative morbidity. We hypothesized that local insufflation of warmed humidified carbon dioxide (CO₂) would maintain wound and core temperature.

Methods Eighty patients undergoing open colon surgery were randomized to standard warming measures, or to additional local wound insufflation of warmed (30 °C) humidified (93 % rH) CO₂ via a gas diffuser. Surface temperature of the open abdominal wound was measured with a heat-sensitive infrared camera, and core temperature was measured with an ear thermometer.

Results Mean operative time was 219 ± 104 and 205 ± 85 min in the CO₂ group and the control group, respectively ($p = 0.550$). Clinical variables did not differ significantly between the groups. The median wound area and wound edge temperatures were 1.2 °C ($p < 0.001$) and 1.0 °C ($p = 0.002$) higher in the CO₂ group, respectively,

than in the control group. The mean core temperature after intubation was the same (35.9 °C) in both groups, but at end of surgery core temperature in the two groups differed, with a mean of 36.2 ± 0.5 °C in the CO₂ group and a mean of 35.8 ± 0.5 °C in the control group ($p = 0.003$).

Conclusions Insufflation of warmed, humidified CO₂ in an open surgical wound cavity prevents intraoperative decrease in surgical wound temperature as well as core temperature.

Introduction

Abdominal surgery under general anesthesia leads to intraoperative hypothermia. This temperature drop is due in part to a shift of the threshold for the thermoregulatory defense mechanism toward lower temperatures imposed by anesthetics [1]. In addition, because of exposure of the patient to ambient air and convection in the relatively cold operating room, evaporation and radiation from the skin and the open surgical wound occurs.

Hypothermia is traditionally defined as a core temperature of ≤ 36 °C. Patient outcomes are reported to be better when a temperature of > 36.5 °C is maintained [2]. Perioperative core hypothermia increases the risk of surgical wound infection [3–5], because it decreases local tissue blood flow and tissue oxygenation [6, 7]. Moreover, it impairs immune function [8, 9], increases perioperative bleeding and transfusion requirements [10], increases the incidence of postoperative shivering and morbid cardiac events [11], and it prolongs hospital stay and increases costs. Growing awareness of the negative consequences of perioperative hypothermia has led to the development of guidelines [12, 13] and to increased use of countermeasures to avoid hypothermia. Widely applied warming strategies

J. M. K. Frey (✉) · P. K. Svenarud · J. A. van der Linden
Department of Molecular Medicine and Surgery,
Department of Cardiothoracic Surgery and Anesthesiology,
Karolinska Institute/Karolinska University Hospital,
171 76 Stockholm, Sweden
e-mail: joana.frey@ki.se

M. Janson · M. Svanfeldt
Department of Clinical Sciences, Interventions and Technology
and Department of Molecular Medicine and Surgery,
Division of Surgery, Karolinska Institute/Karolinska University
Hospital, 171 76 Stockholm, Sweden

include passive insulating measures or, even more effective, active transfer of heat to the body with resistive-heating or forced-air warming blankets, as well as fluid warming systems. Nevertheless, more than one-third of general surgery patients undergoing abdominal operations will be hypothermic on arrival in the postoperative care unit [14, 15].

The possibility to warm the open wound during surgery has so far received little attention. The creation of a CO₂-atmosphere within the surgical wound cavity offers unique possibilities, as CO₂ is a greenhouse gas that will reflect radiant heat from the wound [16, 17]. Moreover, the addition of warmed water vapor may further increase local temperature [18].

The aim of the present study was to investigate whether surface temperature and core temperature in an open surgical wound would be affected by local insufflation of warmed humidified CO₂.

Methods

The Karolinska Hospital Ethical Committee approved the study (696/03 2003-12-08). The procedures followed were in accordance with institutional guidelines. Written informed consent was obtained from all subjects. Eighty adult patients undergoing elective open colon surgery at Karolinska University Hospital between March 2007 and May 2008 were randomized to a CO₂ group ($n = 39$) or a control group ($n = 41$). Randomization was achieved with sealed envelopes, each of which was opened as the patient was being transported to the operation room. All patients were covered with heated blankets in the pre-anesthesia room. The operating room temperature was kept at 20–22 °C, and standard warming measures included maximal heating with forced-air heating blankets over the upper part of the body and whenever possible over the lower part of the body as well (Warm Touch, Mallinckrodt Medical Inc., St. Louis, MO), preheated fluids (37 °C) that were additionally warmed to 39–40 °C via a fluid warmer when given to the patient (HOTLINE, Smiths Medical International Ltd (EMEA), Ashford, UK), and insulation of the limbs and the head.

All patients were given standardized premedication, anesthesia, and analgesia. Paracetamol 1 g orally was given as premedication. After arrival in the operating room all patients, except two in the CO₂ group, received a thoracic epidural catheter between vertebrae Th9 and Th12. A 3 ml test dose of Marcain 5 mg/ml + epinephrine 5 µg/ml (AstraZeneca AB, Södertälje, Sweden) was immediately given, after which an infusion of “Breiviks mix” (bupivacain 1 mg/ml + fentanyl 2 µg/ml + epinephrine 2 µg/ml, Apoteket AB, Stockholm, Sweden) was started at a rate of 12–15 ml/h. Anesthesia was induced with fentanyl (B. Braun Medical AB, Danderyd,

Sweden) 1–2 µg/kg, propofol (B. Braun Medical AB, Danderyd, Sweden) 1–2 mg/kg, and atracurium (Glaxo-SmithKline AB, Solna, Sweden), 0.5 mg/kg or rocuronium (Schering-Plough AB, Stockholm, Sweden) 0.6 mg/kg, and continued with inhalation of Sevoflurane (Baxter Medical AB, Kista, Sweden). Phenylephrine or norepinephrine was given i.v. at the discretion of the individual anesthetist to keep a mean blood pressure above 70 mmHg. Atracurium or rocuronium was given intermittently during the operation to keep a train of four value of 0, and reversed with neostigmin 50 µg/kg + glycopyrron 10 µg/kg (Meda AB, Solna, Sweden).

Intraoperatively, all patients received fluids i.v. according to a standardized protocol: glucose 25 mg/ml (Glukos Buffrad, Baxter, Kista, Sweden) 1 ml/kg per h, hydroxyethyl starch 60 mg/ml (Voluven, Fresenius Kabi AB, Uppsala, Sweden), 2 ml/kg per h, and Ringer’s acetate 2 ml/kg per h (Baxter Medical AB, Kista, Sweden). Additional Voluven or Ringer’s acetate was given if the attending anesthetist diagnosed hypovolemia. Transfusions were given at the discretion of the attending anesthetist.

Six senior surgeons participated in the trial, and they all used a circular abdominal wall retractor (GO400/GO450 General Retractor System, Omni-Tract Surgical, St. Paul, MN). The competence of the bowel anastomosis was, whenever applicable, tested by filling the abdominal cavity with approximately 200 ml of preheated (37 °C) saline (0.9 %), followed by insufflation of air into the rectum. The fluid was thereafter removed with a suction device. According to the guidelines at our hospital, patients needed to have a core temperature of ≥ 36 °C before being extubated.

Patients randomized to the CO₂ group received insufflation of warmed humidified CO₂ into the open wound cavity. Dry medical CO₂ was delivered at a flow rate of 10 l/min at a pressure of 4.5 bar from a pressurized gas cylinder (AGA gas AB, Stockholm, Sweden) via a 1/4 in. (6.35 mm) PVC tube to a plastic bottle containing sterile water (Hudson Oxygen humidifier without jet adaptor, Meteko Instrument AB, Esbo, Finland), which humidified the passing CO₂. The bottle was submerged in a heated water bath (Water thermostat-bath WB-4MS, BioSan, Riga, Latvia), which was kept at 40 °C. The humidified and warmed CO₂ then passed through a 2.5 m long PVC tube with polyurethane foam at its end (CarbonAid gas diffuser, Cardia Innovation AB, Stockholm, Sweden). The cylindrical polyurethane foam tip diverts the gas jet into multiple directions via the many small paths inside the foam. The gas is thus uniformly distributed, and the large diffuser surface area greatly reduces the velocity of the outflow [19, 20]. The CO₂ delivered to the patient had a temperature of 30 °C and a relative humidity of 93 %. The gas diffuser was positioned inside the open abdominal wound

cavity (in the right cranial quadrant) at a depth of approximately 4 cm from the skin as soon as the surgeon had fixed the wound edges with the circular abdominal wall retractor. Two additional abdominal retracting pads, each consisting of a flat metal rod enclosed in polyurethane foam measuring $4.5 \times 4.5 \times 5$ cm (Disarp, Unomedical A/S, Birkerød, Denmark), were then positioned around the abdominal wound edge to increase the depth of the surgical wound cavity. Insufflation of warmed humidified CO₂ was thereafter started and continued until the abdominal retractor and the retracting pads were removed, just before surgical closure of the wound.

The temperature in the wound cavity was measured with a heat-sensitive infrared camera (ThermaCAM B2, FLIR Systems AB, Danderyd, Sweden). This camera gives a temperature image of the observed area. Single shot images (160×120 pixels) can be stored, whereby the device stores each pixel of the image together with its corresponding temperature. Thus, when a thermographic image is being captured, the temperatures of all the pixels in the image area are registered. The camera was mounted on a rigid pod 1 m above the wound to ensure that all images from each patient showed the wound surface area from the same position. Images were taken every tenth minute, beginning just before the surgical incision and concluding when the wound was closed. The images were later analyzed with a software program (ThermaCAM Researcher Basic 2.8 SR-1, FLIR Systems AB, Danderyd, Sweden), which allows delineation of the wound cavity. The mean wound temperatures during the operation are presented for every thirtieth min, based on the mean of the three images captured during this time interval. Core temperature was measured in degrees Celsius at the tympanic membrane every thirtieth min with a thermometer (CORE-CHECK Tympanic Thermometer System, Cardinal Health, Dublin, OH) from the time the patient was anesthetized until the end of surgery. The temperatures are presented for every thirtieth min for the first 3 h only, as thereafter fewer than 50 % of the patients were available for comparison. The median group temperatures were calculated by using the median temperature for each patient during the operation—i.e., the area under the curve. Thus, the problems of analyzing repetitive measurement as well as differences in operative time among the patients were avoided.

Statistical analysis

Based on the power calculations the study required at least 69 patients in total to achieve statistical power of 90 % with an alpha of 0.05 to detect a core temperature difference of 0.5 °C (± 1.0). Results were analyzed with SPSS for Windows version 15.0 (Lead Technologies Inc., Chicago, IL). Data are presented as means $\pm$ SD when normally

distributed or otherwise as medians and 25th/75th percentiles. Student's *t*-test, the chi-square test, Fisher's exact test, the Mann–Whitney *U*-test, or the Wilcoxon tests were used when appropriate. Differences were considered to be statistically significant if $p < 0.05$.

Results

Eighty patients were initially randomized, 41 to the CO₂ group and 39 to the control group (Fig. 1). Six patients were excluded before statistical analysis, three from the CO₂ group and three from the control group, leaving 74 to be analyzed. In two excluded patients, one from each group, the technical quality of the thermographic images did not allow temperature measurements. One patient randomized to the control group was excluded because of preoperative fever (38.0 °C). So was a patient originally randomized to the CO₂ group, who underwent liver resection and had most of the wound cavity covered with a plastic film during the procedure. Finally, two patients were excluded, one from each group, because they were accidentally found to be lying on a warm air mattress intraoperatively (KANMED WarmCloud, KANMED AB, Bromma, Sweden), and one of them received first-degree burns on one of his heels. This heating device was thereafter not used in our department.

There were no significant differences between the two groups in age, gender, weight, height, or body mass index (BMI) (Table 1). Neither were there significant differences between the groups regarding patients' diagnoses or operation codes. Intraoperative variables are listed in Table 2. Forced air heating blankets covered the upper part of the body in all patients and the lower part of the body in 61–63 % in both groups. The abdominal cavity was rinsed with a small amount of saline almost equally often in both groups. The mean operative time was similar in the two groups, with 219 ± 104 and 205 ± 85 min for the CO₂ group and the control group, respectively ($p = 0.550$). Hospital stay and volume of intraoperative bleeding did not differ significantly between the groups. However, patients in the CO₂ group were extubated 8 min earlier compared than patients in the control group ($p = 0.035$).

The median wound area temperatures were 31.1 °C in the CO₂ group and 29.9 °C in the control group ($p < 0.001$), and the median wound edge temperature was 29.5 °C in the CO₂ group and 28.5 °C in the control group ($p = 0.002$). Also, the mean core temperature after intubation was the same (35.9 °C) in both groups, but at end of surgery the two groups differed significantly, with 36.2 °C in the CO₂ group and 35.8 °C in the control group ($p = 0.003$). In accordance with this finding, the median core temperature was 0.5 °C higher in the CO₂ group

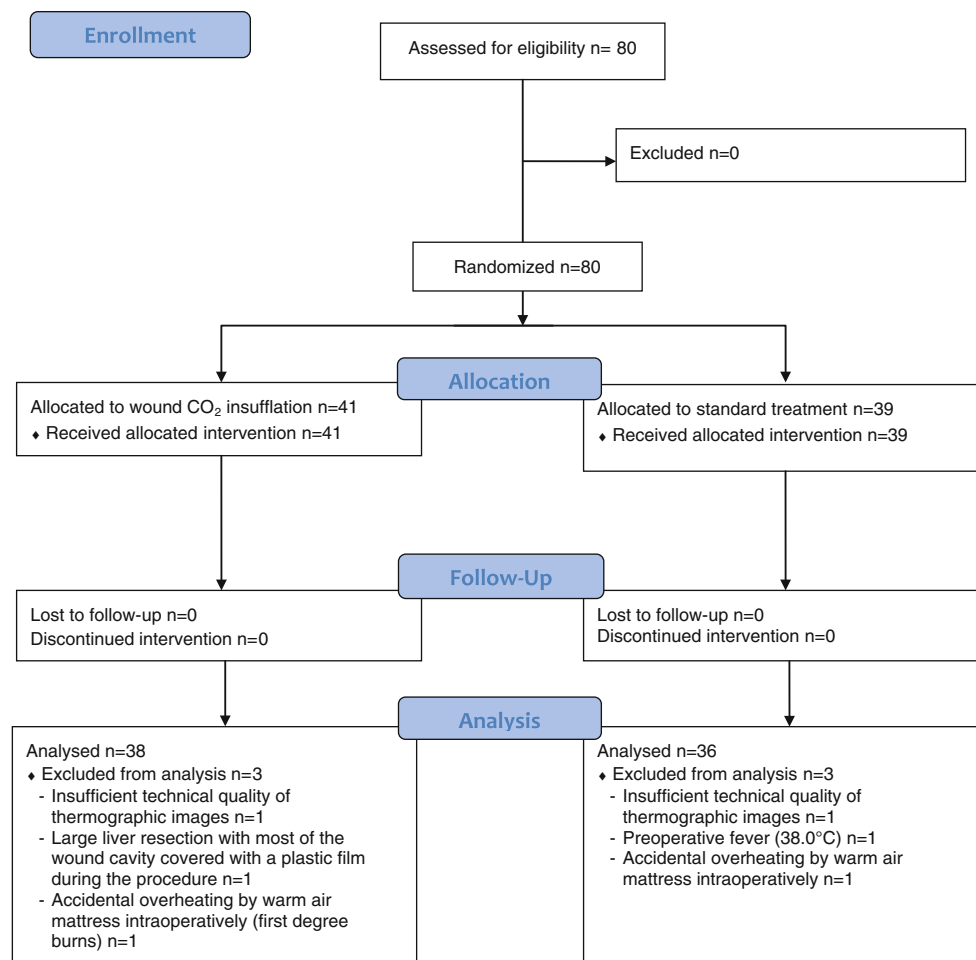


Fig. 1 Study flow diagram

during the operation (Table 3). The mean wound area, wound edge, and core temperatures for the two groups during the first 3 h of surgery are shown in Fig. 2. At end of surgery 55 % (20/36) of the patients in the control group had a core temperature <36 °C compared with 24 % (9/38) in the treatment group ($p < 0.01$).

Discussion

Over the last two decades, an increasing number of abdominal operations are being done with minimally invasive or laparoscopic techniques. The latter technique has several advantages including that it prevents exposure of the internal tissues to ambient dry and cold air and airborne contamination. Instead, dry CO₂ is usually insufflated as a jet through a thin port into the peritoneal cavity. The high solubility of CO₂ explains why this gas will cause much less harm than air if it is unintentionally introduced into the venous or arterial system. Many animal and clinical studies have been undertaken to investigate if the

insufflated dry CO₂ jet causes local desiccation of the peritoneum and promotes local inflammation and whether such effects can be prevented by humidification. Based on the results of these studies, many centers now use commercially available techniques to apply warmed and humidified CO₂ during laparoscopic surgery.

We had several reasons to investigate the effects of warmed and humidified CO₂ during open abdominal surgery in patients. First, the clinical application of humidified warmed gas is common in laparoscopic surgery. Second, the technique is clinically used in cardiothoracic surgery. Furthermore, perioperative core hypothermia has been associated with a worse clinical outcome: i.e., increased risk of surgical wound infection [3–5], morbid cardiac events [11], as well as prolonged hospital stay and increased costs. Despite growing awareness of the negative consequences of perioperative hypothermia more than one-third of general surgery patients undergoing abdominal operations will be hypothermic when they arrive in the postoperative care unit [14, 15]. Because the rate of surgical site infection is 5–10 times higher in open colon surgery compared with

Table 1 Group characteristics (mean $\pm$ SD, or number of patients and percentage)

	CO ₂ group (<i>n</i> = 38)	Control group (<i>n</i> = 36)	<i>p</i> value
Age, years	61 $\pm$ 14	66 $\pm$ 19	0.222 [†]
Sex, %			
Male	21 (55)	23 (64)	0.486 [†]
Female	17 (45)	13 (36)	
Length, m	1.72 $\pm$ 0.1	1.68 $\pm$ 0.1	0.132 [‡]
Weight, kg	76 $\pm$ 14	73.6 $\pm$ 22	0.554 [‡]
BMI, kg/m ²	25.8 $\pm$ 4	25.7 $\pm$ 6	0.978 [‡]
Diagnosis, %			
Cancer	25 (66)	24 (67)	0.936 [§]
Diverticulitis	4 (11)	2 (6)	0.675 [†]
Inflammatory bowel disease	8 (21)	7 (19)	0.863 [§]
Other benign	2 (5)	4 (11)	0.424 [†]
Operation codes, %			
Ileocolic resection	5 (13)	1 (3)	0.200 [†]
Total colectomy	2 (5)	3 (8)	0.670 [†]
Subtotal colectomy	0 (0)	1 (3)	0.486 [†]
Right hemicolectomy	12 (32)	7 (19)	0.232 [§]
Transverse colectomy	0 (0)	1 (3)	0.486 [†]
Left hemicolectomy	1 (3)	2 (6)	0.610 [†]
Sigmoid colectomy	6 (16)	4 (11)	0.737 [†]
High anterior resection	3 (8)	3 (8)	1.000 [†]
Proctocolectomy	2 (5)	0 (0)	0.494 [†]
Rectal resection	3 (8)	4 (11)	0.707 [†]
Rectal amputation	2 (5)	3 (8)	0.670 [†]
Surgical treatment of intra-abdominal	2 (5)	4 (11)	0.424 [†]
Adherences	4 (11)	2 (6)	0.675 [†]
Partial small bowel resection	3 (8)	3 (8)	1.000 [†]
Colostomy	2 (5)	3 (8)	0.670 [†]
Sigmoidostomy	1 (3)	4 (11)	0.194 [†]
Ileostomy	2 (5)	0 (0)	0.494 [†]
Colostomy closure	1 (3)	0 (0)	0.486 [†]
Koch's pouch	2 (5)	3 (8)	0.670 [†]
Small pelvic reservoir	2 (5)	0 (0)	0.494 [†]
Cholecystectomy	1 (3)	0 (0)	0.486 [†]
Nephrectomy	3 (8)	1 (3)	0.615 [†]
Partial liver resection	1 (3)	1 (3)	1.000 [†]
Salpingo-oophorectomy	0 (0)	1 (3)	0.486 [†]
Hysterectomy	1 (3)	1 (3)	1.000 [†]
Closure of colostomy hernia	1 (3)	1 (3)	1.000 [†]

A patient undergoing a procedure may receive several operation codes

[†] Fisher's exact test; [‡] *t*-test;

[§] χ^2 test

cardiothoracic surgery, the potential impact of the technique is much greater in open colon surgery. Finally, the technique opens a new way to protect exposed tissues in open surgical wounds. Where such a vital parameter as local temperature has hardly been studied in humans, any change in local temperature and, indirectly, in core temperature will affect local tissue perfusion and vice versa.

As far as we know this is the first study evaluating open wound temperature when exposing the internal abdominal

tissues to ambient air in the operating room. Moreover, when the open abdominal wound was exposed to humidified warmed CO₂, the median surgical wound area temperature increased significantly from 29.9 to 31.1 °C. It is not known what the optimal wound temperature is during open surgery or if the noted increase is of clinical importance. As the normal temperature of the abdominal viscera is assumed to be close to the core temperature of 37 °C in a normothermic healthy adult, one may assume that a tem

Table 2 Intraoperative variables and hospital stay (mean $\pm$ SD, median with 25th/75th percentile, or *n* and percentage)

	CO ₂ group (<i>n</i> = 38)	Control group (<i>n</i> = 36)	<i>p</i> value
Forced-air heating blankets covering, %			
Upper part of the body	38 (100)	36 (100)	1.000 [†]
Lower part of the body	24 (63)	22 (61)	0.856 [†]
Abdominal cavity rinsing, <i>n</i>	17 (45)	17 (47)	0.831 [†]
Operative time, min	219 $\pm$ 104	205 $\pm$ 85	0.550 [‡]
Intraoperative bleeding, ml	325 (137.5/525)	300 (100/575)	0.992*
Time from end of surgery to extubation, min	18 $\pm$ 8	26 $\pm$ 21	0.035 [‡]
Hospital stay, days	9.5 (7/15)	9 (7/14)	0.895*

* Mann–Whitney *U*-test; [†] Fisher's exact test; [‡] *t*-test

Table 3 Intraoperative temperatures (mean $\pm$ SD, or median with 25th/75th percentile)

	CO ₂ group (<i>n</i> = 38)	Control group (<i>n</i> = 36)	<i>p</i> value
Wound area temperature during surgery, °C (median AUC)	31.1 (29.9/31.7)	29.9 (29.3/30.4)	<0.001 [†]
Wound edge temperature during surgery, °C (median AUC)	29.5 (28.4/30.5)	28.5 (27.7/29.3)	0.002 [†]
Core temperature, °C			
After intubation	35.9 $\pm$ 0.5	35.9 $\pm$ 0.4	0.877*
At start of surgery	35.6 $\pm$ 0.5	35.5 $\pm$ 0.6	0.252*
At end of surgery	36.2 $\pm$ 0.5	35.8 $\pm$ 0.5	0.003*
Core temperature during surgery, °C (median AUC)	36.0 (35.6/36.2)	35.5 (35.4/36.0)	0.028 [†]

AUC area under the curve

* *t*-test; [†] Mann–Whitney *U*-test

perature increase toward normal is advantageous. The relatively small local temperature increase in this study may be explained by the heating system used. It delivered not fully humidified CO₂ at 30 °C, and this calls for technical improvement of the heating system.

Nevertheless, insufflation of humidified CO₂ helped to improve the median core temperature to 36.0 °C in the CO₂ group during the operation, which was 0.5 °C higher than the core temperature in the control group. The difference may seem small, but even mild hypothermia reduces leukocyte function [9]. In a randomized study, patients undergoing colon surgery with an average 1.9 °C fall in core temperature had a threefold risk of surgical wound infection and prolonged hospitalization over the reduction that occurred patients who were actively kept normothermic [3]. Hypothermia also causes hypertension in elderly patients and individuals at high risk for cardiac complications [21]. In high-risk heart patients a slight fall in core temperature by only 1.3 °C implied a threefold higher risk of adverse myocardial outcomes [11]. Even a mild drop in core temperature (<1 °C) significantly increases blood loss and increases the relative risk for transfusion [10]. The vasoconstriction-induced tissue hypoxia may also decrease the strength of the healing wound independent of its ability

to reduce resistance to infection [22]. When using the traditional definition of hypothermia—i.e., a core temperature of less than 36 °C—55 % of the patients in the control group were hypothermic at end of surgery compared with 24 % in the treatment group (*p* < 0.01). It may still be argued that a median difference in core temperature between the groups of 0.5 °C is rather modest, but the core temperature in some patients in the control group dropped down to 34 °C. To what extent the attained 0.5 °C median difference in core temperature can be proved to make a difference in objective outcome data remains to be settled in a much larger study, but at least patients in the treatment group were extubated significantly earlier. Moreover, any awake patient will feel distressed and be prone to shivering when subjected to mild core hypothermia (<36.0 °C). Because of the recognized drawbacks of perioperative hypothermia, centers usually have to follow international guidelines [12, 13], and some insurers reduce reimbursement if perioperative hypothermia is not prevented.

This clinical study evaluated the heating effect of warmed humidified CO₂ gas on surface and core temperature in an open wound during a complete surgical procedure. Earlier experimental work indicates that CO₂ should be delivered via a gas diffuser from within a wound

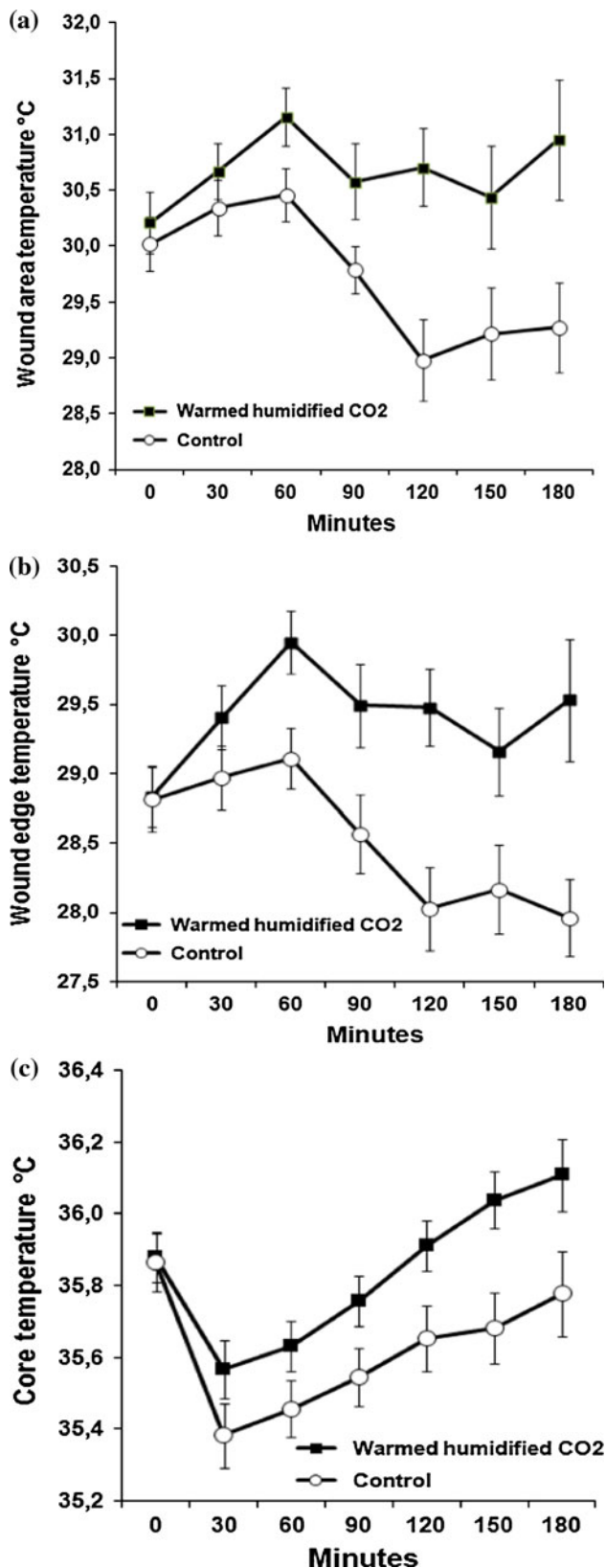


Fig. 2 Mean wound area (a), wound edge (b), and core (c) temperatures for the two groups during the first 3 h of surgery

cavity to create an atmosphere close to 100 % CO₂ [23]. We included patients undergoing open colon surgery, since that type of surgery involves a large, deep wound cavity. The method can, however, be used in more or less any open surgical procedure, provided that a cavity is created around the open wound surface—e.g. by creating a rim around the wound edges. Only a continuous high inflow (10 l/min) of CO₂ is able to counteract the strong force of diffusion of surrounding air into the open wound cavity [19, 24].

When the greenhouse gas CO₂, which is heavier than air, is insufflated with a laminar flow, it tends to settle in the wound cavity like a protective layer. This minimizes the convective air currents caused by the operating room ventilation [20]. A local atmosphere of CO₂ in the open wound has been shown to have an insulating effect, both experimentally [17, 18] and clinically [16]. The addition of warmed water vapor to CO₂ prevents evaporation from the open wound and the cooling effect that otherwise would have occurred [17, 18]. Warmed humidified CO₂ has a much higher heat capacity than warmed dry CO₂, and it promotes heat transfer to tissues. In addition, water vapor itself is a greenhouse gas.

At normal core temperature, CO₂ has a bacteriostatic effect compared with a logarithmic bacterial growth rate in air. This is not only a result of an O₂-deficit but is mainly due to a specific CO₂-effect, which is dependent on a high CO₂ concentration [25]. Moreover, the continuous overflow of CO₂ from the wound opening has in an experimental study been shown to repel and transport particles away from the wound and thus prevent direct airborne contamination with approximately 80 % [26]. The first few hours following bacterial contamination constitute a decisive period during which infection is established. The effects of hypothermia-induced hypoperfusion are especially important during the intraoperative period. Techniques aimed at improving resistance to surgical wound infection are thus most likely to succeed if implemented intraoperatively [27].

Hypothermia triggers thermoregulatory vasoconstriction, which decreases subcutaneous oxygen tension [5, 7]. Also, hypothermia (and low levels of CO₂) shifts the oxygen saturation curve to the left, whereby hemoglobin increases its affinity to oxygen, and thus tissue oxygen tension is reduced. Conversely, an increase in CO₂ and temperature (The Bohr effect) causes a rightward shift that reduces the affinity of hemoglobin to oxygen and improves tissue oxygen tension. Several clinical studies have found that the incidence of postoperative wound infections correlates with intraoperative subcutaneous oxygen tension [28, 29]. Subcutaneous tissue is particularly vulnerable to vasoconstriction, since there is little regulation of blood flow, except in response to locally applied heat [7, 30].

Because anesthesia causes vasodilatation, heat is more easily redistributed from the core out to the wound surface. The lower the surface temperature, the greater the core-to-peripheral temperature gradient and thus the rate of heat redistribution and heat loss. The opposite occurs if the wound surface temperature is warmed. In that case, the heat will redistribute to deeper compartments within the body and core temperature will increase, and thus the risk of wound infection may be attenuated. In open surgical wounds, radiative heat loss, and in particular evaporative heat loss, can be substantial [31]. Considering the well-known negative effects of hypothermia, it seems prudent to keep both the patient and the surgical wound at normothermia. Even if the patient is well protected, there will still be a substantial heat loss from the unprotected open surgical wound. A warmed, humidified CO₂ atmosphere provides effective thermal insulation of the open surgical wound, and the resulting increase in wound and core temperature may help to reduce the negative consequences of mild hypothermia.

The study was not designed to evaluate the incidence of surgical site infections. Such a study would have needed many more patients, preferably with a more effective heating setup. For example, assuming a power of 80 %, a type I error of 0.05, and that the method would half the surgical site infection rate from 5 to 2.5 % or from 10 to 5 %, 1,806 and 864 patients, respectively, would have to be recruited to a large multicenter trial involving major colon surgery. Because the 74 included patients of our study represent less than 10 % of the number of patients needed, we did not think it made sense to study the surgical site infection rate. Moreover, the operating team was not blinded to type of treatment, since the surgical team immediately sensed the insufflated warmed humidified CO₂ in the surgical wound with their hands, and the insufflation was heard by all personnel in the operating room. Also, we did not focus on airborne contamination in this study, since it is a very problematic issue to study during ongoing surgery.

It may be argued that we should first have applied an animal model to study tissue oxygen levels at the wound edge or at wound infection or wound healing, since they correlate with the perfusion and thus the temperature of the wound. Lowering of local wound tissue and edge temperatures as well as core temperature (core hypothermia) will directly and indirectly cause vasoconstriction, hypoperfusion, local hypoxia, and thus increase the risk of surgical site infection. A big drawback of animal wound infection and healing models is that the wound tissue is always much better perfused/oxygenated in animals than in humans, the animals lack the usually thick and not well perfused subcutaneous fat layer of humans. Furthermore, any point measurement of wound oxygenation would be invasive and

local, whereas infrared temperature measurements indirectly measure the perfusion of the whole wound area, including edges.

As for the method's impact on the global environment, medical CO₂ is a recycled by-product from beer and fertilizer production. If not recovered, medical CO₂ would be vented to the atmosphere. Thus, the CO₂ used does not contribute to extra CO₂ being released into the earth's atmosphere.

In summary, insufflation of warmed, humidified CO₂ in an open surgical wound preserves both the surgical wound temperature and the patient's core temperature.

Acknowledgments Financial support for this work was provided by the Karolinska Institute, and through a regional agreement on medical training and clinical research (ALF) between the Stockholm county council and the Karolinska Institute, Stockholm, Sweden. Professor van der Linden is a shareholder of Cardia Innovation AB (Stockholm, Sweden), which provided gas diffusers free of charge for the study. Registration number: NTC01213628 (www.clinicaltrials.gov). The authors are grateful to Kristina Kilsand for excellent technical assistance.

References

1. Sessler DI (2008) Temperature monitoring and perioperative thermoregulation. *Anesthesiology* 109:318–338
2. Young VL, Watson ME (2006) Prevention of perioperative hypothermia in plastic surgery. *Aesthet Surg J* 26:551–571
3. Kurz A, Sessler DI, Lenhardt R (1996) Perioperative normothermia to reduce the incidence of surgical-wound infection and shorten hospitalization. *N Engl J Med* 334:1209–1215
4. Melling AC, Ali B, Scott EM et al (2001) Effects of preoperative warming on the incidence of wound infection after clean surgery: a randomised controlled trial. *Lancet* 358:876–880
5. Sessler DI (2001) Complications and treatment of mild hypothermia. *Anesthesiology* 95:531–543
6. Greif R, Akca O, Horn EP et al (2000) Supplemental perioperative oxygen to reduce the incidence of surgical-wound infection. Outcomes Research Group. *N Engl J Med* 342:161–167
7. Sheffield CW, Sessler DI, Hopf HW et al (1996) Centrally and locally mediated thermoregulatory responses alter subcutaneous oxygen tension. *Wound Rep Reg* 4:339–345
8. Beilin B, Shavit Y, Razumovsky J et al (1998) Effects of mild perioperative hypothermia on cellular immune responses. *Anesthesiology* 89:1133–1140
9. Wenisch C, Narzt E, Sessler DI et al (1996) Mild intraoperative hypothermia reduces production of reactive oxygen intermediates by polymorphonuclear leukocytes. *Anesth Analg* 82:810–816
10. Rajagopalan S, Mascha E, Na J et al (2008) The effects of mild perioperative hypothermia on blood loss and transfusion requirement. *Anesthesiology* 108:71–77
11. Frank SM, Fleisher LA, Breslow MJ et al (1997) Perioperative maintenance of normothermia reduces the incidence of morbid cardiac events. A randomized clinical trial. *J Am Med Assoc* 277:1127–1134
12. Radauceanu DS, Dragnea D, Craig J (2009) NICE guidelines for inadvertent peri-operative hypothermia. *Anaesthesia* 64:1381–1382
13. Sessler DI (2009) New surgical thermal management guidelines. *Lancet* 374:1049–1050

14. Forbes SS, Eskicioglu C, Nathens AB et al (2009) Evidence-based guidelines for prevention of perioperative hypothermia. *J Am Coll Surg* 209:492–503
15. Hedrick TL, Heckman JA, Smith RL et al (2007) Efficacy of protocol implementation on incidence of wound infection in colorectal operations. *J Am Coll Surg* 205:432–438
16. Frey JM, Svegby HK, Svenarud PK et al (2010) CO₂ insufflation influences the temperature of the open surgical wound. *Wound Rep Reg* 18:378–382
17. Persson M, Elmqvist H, van der Linden J (2004) Topical humidified carbon dioxide to keep the open surgical wound warm: the greenhouse effect revisited. *Anesthesiology* 101: 945–949
18. Persson M, van der Linden J (2005) Can wound desiccation be averted during cardiac surgery? An experimental study. *Anesth Analg* 100:315–320
19. Persson M, van der Linden J (2003) De-airing of a cardiothoracic wound cavity model with carbon dioxide: theory and comparison of a gas diffuser with conventional tubes. *J Cardiothorac Vasc Anesth* 17:329–335
20. Persson M, Svenarud P, van der Linden J (2004) What is the optimal device for carbon dioxide deairing of the cardiothoracic wound and how should it be positioned? *J Cardiothorac Vasc Anesth* 18:180–184
21. Frank SM, Higgins MS, Breslow MJ et al (1995) The catecholamine, cortisol, and hemodynamic responses to mild perioperative hypothermia. A randomized clinical trial. *Anesthesiology* 82:83–93
22. Prockop DJ, Kivirikko KI, Tuderman L et al (1979) The biosynthesis of collagen and its disorders (first of two parts). *N Engl J Med* 301:13–23
23. Persson M, van der Linden J (2003) A simple system for intraoperative antiseptic wound ventilation. *J Hosp Infect* 55:152–153
24. Svenarud P, Persson M, van der Linden J (2003) Intermittent or continuous carbon dioxide insufflation for de-airing of the cardiothoracic wound cavity? An experimental study with a new gas-diffuser. *Anesth Analg* 96:321–327
25. Persson M, Svenarud P, Flock JI et al (2005) Carbon dioxide inhibits the growth rate of *Staphylococcus aureus* at body temperature. *Surg Endosc* 19:91–94
26. Persson M, van der Linden J (2004) Wound ventilation with carbon dioxide: a simple method to prevent direct airborne contamination during cardiac surgery? *J Hosp Infect* 56:131–136
27. Gottrup F (2000) Prevention of surgical-wound infections. *N Engl J Med* 342:202–204
28. Greif R, Sessler DI (2004) Supplemental oxygen and risk of surgical site infection. *J Am Med Assoc* 291:79–87
29. Hopf HW, Hunt TK, West JM et al (1997) Wound tissue oxygen tension predicts the risk of wound infection in surgical patients. *Arch Surg* 132:997–1005
30. Rabkin JM, Hunt TK (1987) Local heat increases blood flow and oxygen tension in wounds. *Arch Surg* 122:221–225
31. Sessler DI (2000) Perioperative heat balance. *Anesthesiology* 92:578–596