Anesthesiology 2006; 104:944–9

Mild Hypercapnia Increases Subcutaneous and Colonic Oxygen Tension in Patients Given 80% Inspired Oxygen during Abdominal Surgery

Edith Fleischmann, M.D., Friedrich Herbst, M.D.,† André Kugener, M.D.,‡ Barbara Kabon, M.D.,* Monika Niedermayr, M.D.,* Daniel I. Sessler, M.D.,§ Andrea Kurz, M.D.‖*

Background: **Supplemental perioperative oxygen increases tissue oxygen tension and decreases incidence of wound infection in colorectal surgery patients. Mild intraoperative hypercapnia also increases subcutaneous tissue oxygen tension. However, the effect of hypercapnia in patients already receiving supplemental oxygen is unknown, as is the effect of mild hypercapnia on intestinal oxygenation in humans—although the intestines are presumably the tissue of interest for colon surgeries. The authors tested the hypothesis that mild intraoperative hypercapnia increases both subcutaneous tissue and intramural intestinal oxygen tension in patients given supplemental oxygen.**

Methods: **Patients undergoing elective colon resection were randomly assigned to normocapnia (n = 15, end-tidal carbon dioxide tension 35 mmHg) or mild hypercapnia (n = 15, end-tidal carbon dioxide tension 50 mmHg). Intraoperative inspired oxygen concentration was 80%. The authors measured subcutaneous tissue oxygen tension in the right upper arm and intramural oxygen tension in the left colon. Measurements were averaged over time within each patient and, subsequently, among patients. Data were compared with chi-square, unpaired *t*, or Mann–Whitney rank sum tests; $P < 0.05$ was significant.**

Results: **Morphometric characteristics and other possible confounding factors were similar in the groups. Intraoperative tissue oxygen tension in hypercapnic patients was significantly greater in the arm (mean ± SD: 116 ± 29 mmHg *vs.* 84 ± 25 mmHg; $P = 0.006$) and colon (median [interquartile range]: 107 [81–129] *vs.* 53 [41–104] mmHg; $P = 0.020$).**

Conclusions: **During supplemental oxygen administration, mild intraoperative hypercapnia increased tissue oxygen tension in the arm and colon. Previous work suggests that improved tissue oxygenation will reduce infection risk *via* the proposed pathomechanism, although only an outcome study can confirm this.**

WOUND infections and colonic anastomotic leakage are serious surgical complications.[1,2] Even in patients who are kept normothermic[3] and given 80% oxygen,[4] the incidence of wound infection exceeds 5% after colonic resections. Anastomotic leakage is an especially serious type of wound complication and is relatively common, especially after surgery on the left side of the colon.[2]

Successful surgical wound healing and resistance to wound infection depend critically on adequate tissue perfusion and oxygenation.[4] Tissue oxygen partial pressure is especially important because it enhances oxidative killing by neutrophils.[5] It also augments collagen hydroxylation and thus improves scar formation.[6] Consequently, subcutaneous tissue oxygen tension is an important predictor of surgical wound infection in humans.[7] Similarly, colon tissue oxygen tension correlates with the risk of colonic leakage in rabbit[8] and in humans.[9]

Primary perioperative determinants of tissue oxygen availability include arterial oxygen tension, local perfusion, and cardiac output.[10] For example, supplemental oxygen administration increases subcutaneous[4] and colon tissue oxygentation[11] and decreases the incidence of wound infections in colorectal patients.[4] However, even supplemental oxygen fails to improve tissue oxygenation in hypoperfused tissues.[12] Mild hypercapnia increases perfusion and thus subcutaneous tissue oxygenation[13] in humans by improving cardiac output[14] and inducing vasodilatation.[15] Mild hypercapnia also increases intestinal intramural tissue oxygenation in pigs.[11]

It is unknown whether mild hypercapnia produces a meaningful improvement in tissue oxygenation in patients already given supplemental oxygen, and given the impressive increases produced by supplemental oxygen,[7] it is by no means obvious that hypercapnia will further improve oxygenation. However, more importantly, the effect of mild hypercapnia on intestinal oxygenation in humans remains unknown—although the intestines are presumably the tissue of interest for colon surgery. We therefore tested the hypothesis in a controlled randomized trial that mild intraoperative hypercapnia increases subcutaneous tissue oxygenation and intramural oxygenation in the descending colon in patients given 80% inspired oxygen.

Materials and Methods

With approval of the Medical University of Vienna Institutional Review Board (Vienna, Austria) and written informed consent from the patients, we studied 30 pa-

* Attending, ‡ Research Fellow, Department of Anesthesia and Intensive Care, † Professor, General Surgery, Medical University Vienna. § Chair, Department of Outcomes Research, The Cleveland Clinic; Lolita & Samuel Weakley Professor of Anesthesiology and Director Outcomes Research Institute, University of Louisville. ‖ Professor and Chair, Department of Anesthesiology, University of Bern; Professor and Associate Director, Outcomes Research Institute, University of Louisville.

Received from the Departments of Anesthesia and General Intensive Care and Surgery, Vienna General Hospital, Medical University of Vienna, Vienna, Austria; the Department of Outcomes Research, Cleveland Clinic Foundation, Cleveland, Ohio; the Outcomes Research Institute, Department of Anesthesiology and Perioperative Medicine, University of Louisville, Louisville, Kentucky; and the Department of Anesthesiology, University of Bern, Bern, Switzerland. Submitted for publication October 17, 2005. Accepted for publication January 13, 2006. Supported by grant No. GM 061655 from the National Institutes of Health, Bethesda, Maryland; the Gheens Foundation, Louisville, Kentucky; the Joseph Drown Foundation, Los Angeles, California; and the Commonwealth of Kentucky Research Challenge Trust Fund, Louisville, Kentucky. Mallinckrodt Anesthesiology Products, Inc., St. Louis, Missouri, donated the thermocouples used in this study. None of the authors has a personal financial interest related to this work.

Address correspondence to Dr. Kurz: Department of Anesthesiology, University of Bern, Bern 3010, Switzerland. andrea.kurz@insel.ch. Individual article reprints may be purchased through the Journal Web site, www.anesthesiology.org.

tients with American Society of Anesthesiologists physical status I, II, or III who were undergoing elective colorectal resection for cancer of the left colon between September 2003 and August 2004. Patients were recruited from the operating room schedule on the day before surgery. Exclusion criteria included documented coronary or peripheral artery disease, diabetes mellitus, and any symptoms of infection or bowel obstruction. We also excluded patients with preoperative systolic arterial blood pressure greater than 170 mmHg or diastolic arterial pressure greater than 90 mmHg and patients taking vasoactive drugs.

Protocol

Patients were given a standard mechanical bowel preparation (Klean-Prep®; Norgine, Marburg, Germany; macrogol 3350, polyethylenglycol 59 g) the night before surgery. Patients were allowed to drink until midnight and received 1,000 ml lactated Ringer's solution overnight. Thirty minutes before skin incision, patients were given prophylactic intravenous antibiotic therapy (1.5 g metronidazole and 1.5 g cefuroxime). Anesthesia was induced with fentanyl (1–3 μg/kg), propofol (2–3 mg/kg), and rocuronium (0.6 mg/kg); anesthesia was maintained with sevoflurane adjusted to keep arterial blood pressure within 20% of the preinduction value. Fentanyl was given continuously during surgery at a rate of 3 $\mu g \cdot kg^{-1} \cdot h^{-1}$. No vasoactive drugs were used intraoperatively.

After induction of anesthesia and tracheal intubation, patients were assigned to normocapnia or mild hypercapnia using a set of computer-generated random numbers; assignments were kept in sealed envelopes until used. All patients received 80% oxygen in air. End-tidal carbon dioxide partial pressure was maintained near 35 mmHg (normocapnia) or 50 mmHg (mild hypercapnia). A parallel-group randomized design was used in lieu of a crossover design because there was insufficient time during surgery to test more than one end-tidal carbon dioxide partial pressure. End-tidal carbon dioxide partial pressure was chosen as the end point because it was easy to adjust a patient's carbon dioxide concentration to these levels. The designated end-tidal concentration in the normocapnia group was maintained simply by adjusting the rate of mechanical ventilation with a 10-ml/kg tidal volume and 1–3 l/min fresh gas flow. In the mild hypercapnia group, the soda lime carbon dioxide absorbent was removed from the anesthesia machine. Ventilation was maintained with a 10-ml/kg ideal body weight tidal volume and a respiratory rate of 8 breaths/min. Fresh gas flow was then adjusted to obtain an end-tidal concentration of 50 mmHg. The attending anesthesiologists were aware of group assignment.

Lactated Ringer's solution (500 ml) was given in the recovery room. A bolus of 10 ml/kg lactated Ringer's solution was given before induction of anesthesia. Subsequently, the solution was infused at a rate of 10 $ml \cdot kg^{-1} \cdot h^{-1}$. Blood loss was replaced with colloid (Voluven®, HES 130/0.4, 6%; Fresenius Kabi GmbH, Graz, Austria) at a 1-2:1 ratio; supplemental fluid was given as necessary to maintain urine output of at least 1 $ml \cdot kg^{-1} \cdot h^{-1}$. Because we excluded patients with significant cardiovascular disease, erythrocytes were transfused as necessary to maintain hematocrit at 26% or greater.

Upper-body forced-air warming was used on the left arm and head to keep patients normothermic. However, local heating at the tissue oxygen measurement sites (described in the next section) was avoided.

Measurements

Demographic data, American Society of Anesthesiologists physical status, and duration of surgery were recorded. We also recorded all routine anesthetic, respiratory, and hemodynamic values; fluid administration; and urinary output. Inspired oxygen fraction, oxygen saturation, end-tidal sevoflurane, and carbon dioxide concentrations were measured during anesthesia. Core temperature was measured in the distal esophagus (Mon-a-therm; Tyco-Mallinckrodt Anesthesiology Products, St. Louis, MO). Routine anesthetic measurements were recorded at 10-min intervals throughout the perioperative period.

Forearm-minus-fingertip skin temperature gradients were measured on the right arm as an index of arteriovenous shunt vasoconstriction. Skin temperature gradients correlate well with volume plethysmography.[16] Values exceeding 0°C indicate vasoconstriction and correlate with onset of the core temperature plateau.[17]

After induction of anesthesia, a 20-gauge cannula was inserted into a radial artery. Arterial pressure was measured continuously from this catheter throughout surgery; arterial blood was sampled for gas analysis when bowel tissue oxygen tension was measured (details below).

After induction of anesthesia, a silastic tonometer was inserted in the subcutaneous tissue of the right upper arm to measure tissue oxygen tension and temperature. The tonometer consisted of 15 cm of tubing filled with hypoxic saline; 10 cm of the tube was tunneled in subcutaneously. A Clarke-type oxygen sensor and thermistor (Licox; Gesellschaft für Medizinische Sondensysteme, GmBH, Kiel, Germany) were placed in the subcutaneous portion of the silastic tube. *In vitro* accuracy of these oxygen sensors is ± 3 mmHg for the range from 0 to 100 mmHg and $\pm 5\%$ for 100 to 360 mmHg (in a water bath at 37°C).[18] The oxygen sensor calibration remains stable (within 8% of baseline value for room air) *in vivo* for at least 8 h. Temperature sensitivity of the sensors is 0.255/°C. However, thermistors are incorporated into the probes, and temperature compensation was included in the tissue oxygen tension ($Psqo_2$) calcu-

lations. We calibrated individual oxygen sensors by exposing them to room air (ambient partial pressure of oxygen = 154 mmHg); measurements in air were within 10% of 154 mmHg in all cases. After each investigation, the sensors were again exposed to ambient air to exclude a significant drift of the oxygen sensor; none drifted more than 10% from baseline.

To measure intramural intestinal oxygen partial pressure ($Pimo_2$), the same surgeon inserted oxygen sensors through 20-gauge cannula into a section of descending colon (approximately 20 cm away from the tumor) that was subsequently to be resected. The probes were inserted into the tissue plane between the serosa and mucosa after mobilization of the left colon. In addition, needle temperature probes were inserted adjacent to the oxygen probes (Tyco-Mallinckrodt Anesthesiology Products). To obtain temperature corrected measurements, we adjusted the Licox monitor according to the measured temperature. Care was taken to minimize handling of the intestine and to return the bowel to a neutral position.

All intraoperative measurements except $Pimo_2$ were recorded at 10-min intervals, after an initial 30-min equilibration period. $Pimo_2$ was measured every 60 s for 15 min, starting approximately 1 h after the beginning of surgery. Surgery was discontinued during $Pimo_2$ measurements to enhance reading stability. Upon completion of the measurement period, the measurement sites were inspected for edema or hematoma.

Statistical Analysis

The number of patients required for this trial was estimated as follows: Previous studies suggest that a difference in $Psqo_2$ of approximately 15 mmHg is clinically important. We have previously shown that hypercapnia increases subcutaneous tissue oxygenation by approximately the same amount.[11,13] The standard deviations of $Psqo_2$ values in similar studies range from 10 to 20 mmHg, with an average of 15 mmHg. Assuming a difference of at least 15 mmHg between our two treatment groups, 15 patients in each group provide an 80% power to detect a significant difference between the two groups at an α level of 0.05.

Because intraindividual values were stable during our 15-min measurement period, values repeated over time were first averaged within each patient over the 15-min period of intestinal tissue oxygen measurements and then averaged across each group. Potential confounding factors and outcomes of the study were analyzed with chi-square, unpaired two-sided *t*, or Mann–Whitney rank sum tests. Data that were normally distributed are presented as mean ± SD; others are presented as median (interquartile range). $P < 0.05$ was considered statistically significant.

Results

Intramural intestinal oxygen partial pressure was recorded from all 15 patients in each group; however, data of one patient had to be excluded because of technical problems with the oxygen probe. $Psqo_2$ was only recorded from 12 hypercapnia patients and 14 normocapnia patients. Age, weight, height, and American Society of Anesthesiologists physical status classification were similar in the two groups (table 1). The groups did not differ with regard to duration of surgery, end-tidal sevoflurane concentration, or amount of intraoperative fluid or drugs administered. Core temperatures and urinary output were similar, as well (table 2). Heart rate was significantly higher in the hypercapnia group (76 ± 12 *vs.* 68 ± 9; $P = 0.049$). No edema or hematoma was observed at the intestinal oxygen and temperature measurement sites.

During the entire surgery, arterial carbon dioxide pressure was 54 ± 6 mmHg in the hypercapnia group and 39 ± 3 mmHg in the normocapnia group ($P < 0.001$); arterial oxygen pressure was similar in the two groups. pH was slightly, but significantly, less in the hypercapnia group than in the normocapnia group (7.27 ± 0.05 *vs.* 7.38 ± 0.03; $P < 0.001$). $Psqo_2$ was significantly greater in the hypercapnia group (116 ± 29 mmHg) than in the normocapnia group (84 ± 25 mmHg).

During the measurement period of $Pimo_2$, arterial carbon dioxide pressure was 55 ± 5 mmHg in the hypercapnia group and 40 ± 3 mmHg in the normocapnia group ($P < 0.001$); arterial oxygen pressure was similar in the groups (table 3). $Psqo_2$ was significantly greater in the hypercapnia group (116 ± 29 mmHg) than in the normocapnia group (84 ± 25 mmHg; $P = 0.006$; fig. 1). $Pimo_2$ was significantly greater in patients assigned to hypercapnia (107 [81–129] mmHg) than normocapnia (53 [41–104] mmHg; $P = 0.020$; fig. 2). Subcutaneous and colon temperatures were similar in the groups during these measurements, as were sevoflurane concentration, core temperature, arterial oxygen pressure, and mean arterial pressure (table 3).

Table 1. Demographics and Morphometric Characteristics

	Hypercapnia	Normocapnia	*P* Value
Number	15	15	—
Age, yr	55 ± 12	60 ± 9	0.211
Sex, M/F	11/4	8/7	0.256
Weight, kg	78 ± 11	78 ± 9	0.956
Height, cm	175 ± 13	171 ± 11	0.462
ASA physical status, I/II/III	9/5/1	7/7/1	0.847
BMI, kg/m^2	25.7 ± 3.4	26.7 ± 3.0	0.446
Smoker, > 1 pack/day, yes/no	2/13	2/13	1.000
Preoperative hemoglobin, g/l	14.1 ± 1.5	13.3 ± 1.1	0.140
Preoperative fluid, l	688 ± 259	667 ± 258	0.884

Data are presented as mean ± SD or number of patients.

ASA = American Society of Anesthesiologists; BMI = body mass index.

Table 2. Perioperative Variables

	Hypercapnia	Normocapnia	*P* Value
Sevoflurane end-tidal concentration (during surgery), %	1.5 ± 0.2	1.6 ± 0.3	0.208
Fentanyl, mg	1.1 ± 0.4	1.1 ± 0.4	0.990
Colloid, ml	450 ± 438	469 ± 432	0.923
Crystalloid, ml	3,133 ± 1,233	3,685 ± 1,566	0.387
Estimated blood loss, ml	200 ± 166	350 ± 158	0.044
Urine output, ml	300 (200–600)	650 (500–850)	0.130
Core temperature, °C	36.3 ± 0.5	36.1 ± 0.5	0.261
Duration of anesthesia, h	4.2 ± 1.5	5.0 ± 1.2	0.545
Duration of surgery, h	3.3 ± 1.4	4.1 ± 1.2	0.221

Data are presented as mean ± SD or median (interquartile range).

There was weak correlation between tissue oxygenation in the arm and in the colon ($r = 0.46$, $P = 0.022$; fig. 3).

Discussion

Wound infections are established perioperatively, a period that was identified as "decisive" nearly 50 yr ago.[19] This decisive period explains why perioperative factors influence the incidence of infection even though infections are typically detected days after surgery. Wound infections are still considered a surgical complication, although it is well established that infection risk is related to preexisting diseases and type and duration of surgery, and can be reduced by providing appropriate and timely antibiotics.[20]

Another strong predictor of surgical site infection is subcutaneous oxygenation and perfusion.[7] For example, subcutaneous tissue oxygen values less than 60 mmHg are associated with a wound infection rate exceeding 20%.[7] Furthermore, the leakage rate for anastomoses ranges from 3 to 10%[2] and correlates with tissue oxygenation in the colon. For example, the leakage rate progressively increased to 100% as bowel oxygen tension was reduced to less than 20 mmHg in a rabbit model.[8] Another study in humans showed that perianastomotic oxygen tensions less than 20 mmHg are associated with an extremely high leakage rate.[9]

Our current study extends previous results from animals[11] and confirms that mild hypercapnia substantially improves subcutaneous and colonic oxygenation, even in patients whose tissue oxygenation is already high because they are given 80% inspired oxygen. Specifically, subcutaneous tissue oxygen values were roughly 84 ± 25 mmHg in normocapnic patients given supplemental oxygen. With mild hypercapnia in addition to supplemental oxygen, tissue oxygen tension was 116 ± 29 mmHg, a statistically significant increase. Intramural colon tissue oxygen tension in the hypercapnia group was nearly twice that of the normocapnia group (approximately 53 [41–104] mmHg with normocapnia and 107 [81–129] mmHg with hypercapnia)—an even more important result because the colon is probably the critical tissue determining risk of both infection and wound dehiscence.

However, the issue is not simply the extent to which

Table 3. Physiologic Variables at the Time of Intestinal Oxygen Measurement

	Hypercapnia	Normocapnia	*P* Value
Mean arterial pressure, mmHg	77 ± 7	80 ± 4	0.135
Heart rate, beats/min	76 ± 12	68 ± 9	0.049
End-tidal sevoflurane, %	1.7 ± 0.3	1.7 ± 0.4	0.953
Pa_{O_2}, mmHg	336 ± 54	315 ± 65	0.48
End-tidal P_{CO_2}, mmHg	50 ± 1	35 ± 2	< 0.001
Pa_{CO_2}, mmHg	55 ± 5	40 ± 3	< 0.001
Psq_{O_2}, mmHg	116 ± 29	84 ± 25	0.006
Tsq, °C	34.2 ± 1.2	33.6 ± 1.2	0.203
Pim_{O_2}, mmHg	107 (81–129)	53 (41–104)	0.020
Tgit, °C	35.0 (34.6–35.0)	34.7 (32.6–35.1)	0.314
Core temperature, °C	36.3 ± 0.5	36.1 ± 0.5	0.261
Forearm-minus-finger skin temperature gradient	−0.1 ± 1.2	−0.7 ± 1.8	0.345
Measurement time, min after incision	54 ± 17	73 ± 31	0.055

Analysis reported in this table is restricted to the time of colonic tissue oxygen measurement, a 15-min period starting approximately 1 h after incision. Data are presented as mean ± SD or median (interquartile range).

Pa_{CO_2} = arterial carbon dioxide partial pressure; Pa_{O_2} = arterial oxygen partial pressure; P_{CO_2} = carbon dioxide partial pressure; Pim_{O_2} = intramural tissue oxygen partial pressure in the left colon; Psq_{O_2} = subcutaneous tissue oxygen partial pressure in the upper arm; Tgit = temperature in the intramural tissue of the left colon; Tsq = temperature in the subcutaneous tissue of the upper arm.

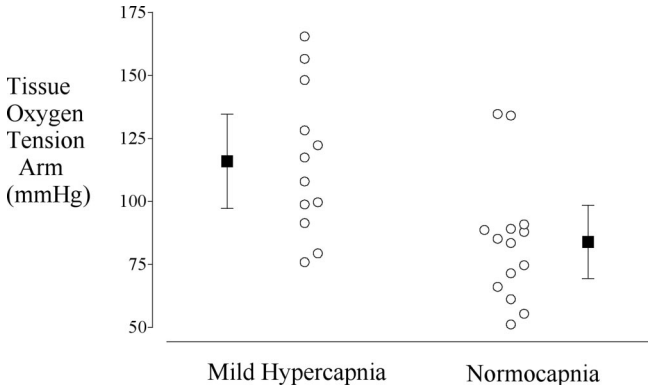

Fig. 1. Subcutaneous oxygen partial pressure in the upper arm during colon resection surgery in patients receiving supplemental oxygen (inspired oxygen concentration of 80%) and an end-tidal carbon dioxide partial pressure of 35 mmHg (normocapnia) and patients receiving supplemental oxygen and a carbon dioxide partial pressure of 50 mmHg (mild hypercapnia). The *open circles* represent the value in each patient. The *squares* show the group means (95% confidence intervals); the group means differed significantly ($P = 0.006$).

hypercapnia improves subcutaneous oxygenation, but also the absolute oxygenation range. Hopf *et al.*[7] showed that subcutaneous tissue oxygen levels greater than 80 mmHg in the postoperative period essentially eliminate surgical wound infections, whereas values less than 40 mmHg are associated with a nearly 50% infection rate in colon surgical patients. Our absolute values of tissue oxygen tension were already relatively high in the normocapnic patients (because of supplemental oxygen administration). Whether an increase beyond 80 mmHg further reduces wound infection is not known, especially in our fairly healthy colon surgical patient population.

In contrast, tissue oxygenation in certain high-risk patient populations remains low even with supplemental oxygen administration. Populations at high risk for wound complications include obese patients,[21] smokers,[22] diabetics,[23] and patients with peripheral vascular

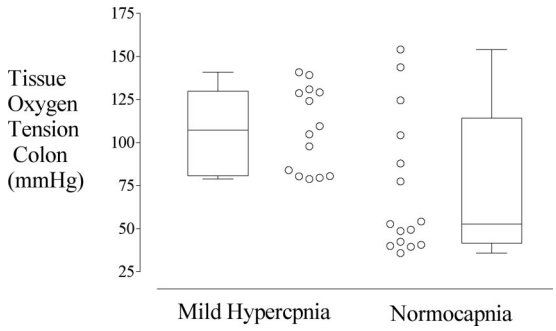

Fig. 2. Intramural oxygen partial pressure in the left colon during colon resection surgery in patients receiving supplemental oxygen (inspired oxygen concentration of 80%) and an end-tidal carbon dioxide partial pressure of 35 mmHg (normocapnia) and patients receiving supplemental oxygen and a carbon dioxide partial pressure of 50 mmHg (mild hypercapnia). The *open circles* represent the value in each patient. Variance is displayed using *box plots* (medians, 25th and 75th quartiles, and ranges); the medians differed significantly ($P = 0.020$).

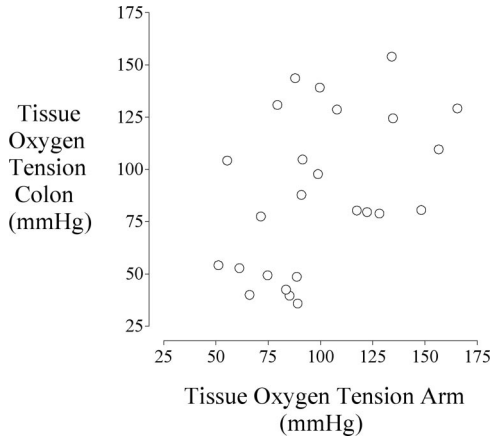

Fig. 3. Correlation between subcutaneous oxygen partial pressure in the upper arm and intramural oxygen partial pressure in the left colon during colon resection surgery. The correlation coefficient was 0.46 ($r = 0.46$, $P = 0.022$).

disease.[24] Therefore, any treatment or treatment combination that increases tissue oxygenation might be beneficial in these patient populations. We recognize that only outcome studies in various populations will determine whether the observed increases in subcutaneous and colonic oxygenation actually reduce infection risk. However, our results suggest that such studies would be worth conducting.

Subcutaneous oxygen partial pressure was measured from a needle-induced surrogate wound in the arm, which is the classic method of evaluating perioperative tissue oxygen tension and has been used in numerous previous studies.[4,7,25] The primary benefit of this location is its convenience and the fact that measurements can be easily conducted during surgery. Microscopic tissue injury to subcutaneous tissues at the sensor insertion site in the upper arm is not only inevitable, but a deliberate feature of the model that is designed to mimic surgical trauma.[26,18] It seems likely this feature contributes to the ability of upper arm oxygenation to predict infection risk.

Placement of the oxygen probes in the intestinal tissue was performed approximately 1 h after incision, when the left colon was mobilized. The probes were inserted into the descending colon (approximately 20 cm away from the tumor) that was subsequently to be resected. One single surgeon, who took special care handling the intestinal tissue, inserted all of the probes. Although we did not observe edema or hematomas at the insertion sites, microscopic tissue injury at the intestinal sensor site is inevitable. Again, this injury should not be considered a limitation of the technique, but a feature that mimics surgical trauma and, thus, more realistically reflects oxygenation that might be observed near an intestinal anastomosis.

We measured colon tissue oxygenation in the descending uninjured colon rather than at the anastomosis directly. We have shown that tissue oxygenation at the

anastomosis is considerably lower in pigs.[27] However, supplemental oxygen administration increased tissue oxygenation significantly at the anastomosis, suggesting that interventions that improve intramural oxygenation in normal intestine are likely to have similar effects at the site of a surgical incision.

Although there was little correlation between tissue oxygenation in the arm and in the colon, both tissues reacted comparably to hypercapnia. This result mirrors those in pigs that were exposed to hypercapnia with and without supplemental oxygen.[11] However, we can probably not make the general assumption that the subcutaneous tissue in the upper arm reflects intestinal tissue and, thus, can be used as a surrogate measurement site. This might especially be the case during certain interventions, *e.g.*, supplemental fluid administration, which affect oxygenation in intestinal tissue, subcutaneous wound tissue, and subcutaneous tissue in the upper arm differently.[28]

A limitation of our study was that we recorded tissue oxygen tension in the left colon only during a brief intraoperative period. It would be of substantial interest to measure tissue oxygenation in the colon and at the anastomosis during the postoperative period. However, it is not currently possible to measure colon tissue oxygenation after the abdomen is closed in humans. Although there was a statistically significant difference in blood loss between normocapnic and hypercapnic patients, it is unlikely that a difference of 150 ml would affect tissue oxygen tension.

In summary, mild intraoperative hypercapnia in patients receiving supplemental oxygen increased tissue oxygen tension in both the arm and the descending colon by amounts that are likely to produce clinically important reductions in infection risk. Therefore, results of the current study suggest that mild hypercapnia may be another inexpensive, low-risk intervention to reduce the incidence of serious and expensive complications—although this proposed pathomechanism awaits confirmation in an outcome trial.

The authors thank Gilbert Haugh, M.S., for the statistical analysis and Nancy Alsip, Ph.D., for editing the manuscript (both of the University of Louisville, Louisville, Kentucky).

References

1. Pryor KO, Fahey TJ III, Lien CA, Goldstein PA: Surgical site infection and the routine use of perioperative hyperoxia in a general surgical population: A randomized controlled trial. JAMA 2004; 291:79–87

2. Moran B, Heald R: Anastomotic leakage after colorectal anastomosis. Semin Surg Oncol 2000; 18:244–8

3. Kurz A, Sessler DI, Lenhardt R: Perioperative normothermia to reduce the incidence of surgical-wound infection and shorten hospitalization. Study of Wound Infection and Temperature Group. N Engl J Med 1996; 334:1209–15

4. Greif R, Akca O, Horn EP, Kurz A, Sessler DI: Supplemental perioperative oxygen to reduce the incidence of surgical-wound infection. Outcomes Research Group. N Engl J Med 2000; 342:161–7

5. Babior BM: Oxygen-dependent microbial killing by phagocytes (first of two parts). N Engl J Med 1978; 298:659–68

6. Prockop DJ, Kivirikko KI, Tuderman L, Guzman NA: The biosynthesis of collagen and its disorders: Part one. N Engl J Med 1979; 301:13–23

7. Hopf HW, Hunt TK, West JM, Blomquist P, Goodson WH III, Jensen JA, Jonsson K, Paty PB, Rabkin JM, Upton RA, von Smitten K, Whitney JD: Wound tissue oxygen tension predicts the risk of wound infection in surgical patients. Arch Surg 1997; 132:997–1004

8. Shandall A, Lowndes R, Young HL: Colonic anastomotic healing and oxygen tension. Br J Surg 1985; 72:606–9

9. Sheridan WG, Lowndes RH, Young HL: Tissue oxygen tension as a predictor of colonic anastomotic healing. Dis Colon Rectum 1987; 30:867–71

10. Hopf HW, Jensen JA, Hunt TK: Calculation of subcutaneous tissue blood flow. Surg Forum 1988; 39:33–6

11. Ratnaraj J, Kabon B, Talcott MR, Sessler DI, Kurz A: Supplemental oxygen and carbon dioxide each increase subcutaneous and intestinal intramural oxygenation. Anesth Analg 2004; 99:207–11

12. Gottrup F, Firmin R, Rabkin J, Halliday B, Hunt TK: Directly measured tissue oxygen tension and arterial oxygen tension assess tissue perfusion. Crit Care Med 1987; 15:1030–6

13. Akca O, Doufas AG, Morioka N, Iscoe S, Fisher J, Sessler DI: Hypercapnia improves tissue oxygenation. ANESTHESIOLOGY 2002; 97:801–6

14. Mas A, Saura P, Joseph D, Blanch L, Baigorri F, Artigas A, Fernandez R: Effect of acute moderate changes in arterial carbon dioxide pressure on global hemodynamics and gastric perfusion. Crit Care Med 2000; 28:360–5

15. Boyd O, Grounds RM, Bennett ED: A randomized clinical trial of the effect of deliberate perioperative increase of oxygen delivery on mortality in high-risk surgical patients. JAMA 1993; 270:2699–707

16. Rubinstein EH, Sessler DI: Skin-surface temperature gradients correlate with fingertip blood flow in humans. ANESTHESIOLOGY 1990; 73:541–5

17. Kurz A, Sessler DI, Christensen R, Dechert M: Heat balance and distribution during the core-temperature plateau in anesthetized humans. ANESTHESIOLOGY 1995; 83:491–9

18. Chang N, Goodson WH III, Gottrup F, Hunt TK: Direct measurement of wound and tissue oxygen tension in postoperative patients. Ann Surg 1983; 197:470–8

19. Miles AA, Miles EM, Burke J: The value and duration of defence reactions of the skin to the primary lodgement of bacteria. Br J Exp Pathol 1957; 38:79–96

20. Classen DC, Evans RS, Pestotnik R, Horn SD, Menlove RL, Burke JP: The timing of prophylactic administration of antibiotics and the risk of surgical wound infection. N Engl J Med 1992; 326:281–6

21. Alexander JW, Rahn R: Prevention of deep wound infection in morbidly obese patients by infusion of an antibiotic into the subcutaneous space at the time of wound closure. Obes Surg 2004; 14:970–4

22. Jensen JA, Goodson WH, Hopf HW, Hunt TK: Cigarette smoking decreases tissue oxygen. Arch Surg 1991; 126:1131–4

23. Schneid-Kofman N, Sheiner E, Levy A, Holcberg G: Risk factors for wound infection following cesarean deliveries. Int J Gynaecol Obstet 2005; 90:10–5

24. Haley RW, Culver DH, Morgan WM, White JW, Emori TG, Hooton TM: Identifying patients at high risk of surgical wound infection: A simple multivariate index of patient susceptibility and wound contamination. Am J Epidemiol 1985; 121:206–15

25. Kabon B, Fleischmann E, Treschan T, Taguchi A, Kapral S, Kurz A: Thoracic epidural anesthesia increases tissue oxygenation during major abdominal surgery. Anesth Analg 2003; 97:1812–7

26. Goodson WH, Hunt TK: Development of a new miniature method for the study of wound healing in human subjects. J Surg Res 1982; 33:394–401

27. Kimberger O, Kabon B, Fleischmann E, Kejci V, Kurz A: The effect of supplemental oxygen on anastomotic tissue oxygenation of colon anastomosis (abstract). ANESTHESIOLOGY 2004; 101:A-718

28. Hiltebrand L, Hager H, Pestel G, Ratnaraj J, Kurz A: Aggressive fluid treatment increases subcutaneous but not intestinal tissue oxygenation (abstract). ANESTHESIOLOGY 2004; 101:A-666