SUPPLEMENTAL PERIOPERATIVE OXYGEN TO REDUCE THE INCIDENCE OF SURGICAL-WOUND INFECTION

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ABSTRACT

Background Destruction by oxidation, or oxidative killing, is the most important defense against surgical pathogens and depends on the partial pressure of oxygen in contaminated tissue. An easy method of improving oxygen tension in adequately perfused tissue is to increase the concentration of inspired oxygen. We therefore tested the hypothesis that the supplemental administration of oxygen during the perioperative period decreases the incidence of wound infection.

Methods We randomly assigned 500 patients undergoing colorectal resection to receive 30 percent or 80 percent inspired oxygen during the operation and for two hours afterward. Anesthetic treatment was standardized, and all patients received prophylactic antibiotic therapy. With use of a double-blind protocol, wounds were evaluated daily until the patient was discharged and then at a clinic visit two weeks after surgery. We considered wounds with culture-positive pus to be infected. The timing of suture removal and the date of discharge were determined by the surgeon, who did not know the patient's treatment-group assignment.

Results Arterial oxygen saturation was normal in both groups; however, the arterial and subcutaneous partial pressure of oxygen was significantly higher in the patients given 80 percent oxygen than in those given 30 percent oxygen. Among the 250 patients who received 80 percent oxygen, 13 (5.2 percent; 95 percent confidence interval, 2.4 to 8.0 percent) had surgical-wound infections, as compared with 28 of the 250 patients given 30 percent oxygen (11.2 percent; 95 percent confidence interval, 7.3 to 15.1 percent; $P=0.01$). The absolute difference between groups was 6.0 percent (95 percent confidence interval, 1.2 to 10.8 percent). The duration of hospitalization was similar in the two groups.

Conclusions The perioperative administration of supplemental oxygen is a practical method of reducing the incidence of surgical-wound infections. (N Engl J Med 2000;342:161-7.)

WOUND infections are common and serious complications of surgery. In patients undergoing colorectal surgery, the incidence of wound infection ranges from 9 percent to 27 percent.[1] Surgical-wound infections can prolong hospitalization by 5 to 20 days[2] and substantially increase the cost of care.[1,3] The first few hours after tissue is contaminated by bacteria constitute a critical period during which wound infections are established.[4] Therefore, perioperative factors influence the incidence of infections, even though infections are typically not detected until some days after surgery. The factors that influence the incidence of surgical-wound infection include the site and complexity of surgery,[1] the patient's underlying illness, the use or nonuse of prophylactic antibiotics,[5-7] the patient's temperature during surgery,[2] the presence or absence of hypovolemia,[8,9] the degree to which pain is controlled postoperatively,[10] and the oxygen tension in tissue.[11]

Bactericidal activity of neutrophils is mediated by oxidative killing, a critical defense against surgical pathogens.[12] Oxidative killing is dependent on the production of bactericidal superoxide radicals from molecular oxygen. The rate of this reaction, which is catalyzed by the NADPH-linked oxygenase, is dependent on the partial pressure of oxygen in the tissue. In the case of neutrophils, oxidative killing depends on a partial pressure of oxygen in the range from 0 to more than 300 mm Hg.[13]

All wounds disrupt the local vascular supply as a result of injury and thrombosis of vessels, which cause wounds to be hypoxic as compared with normal tissue.[14] The oxygen tension of wounds is often less than 30 mm Hg.[14] Resistance to infection therefore depends on the partial pressure of oxygen in the wound[11] and can thus potentially be improved by increasing arterial oxygen tension beyond that required to saturate blood. We tested the hypothesis that the supplemental administration of oxygen during the perioperative period decreases the incidence of postoperative wound infections in patients undergoing elective colorectal resection.

METHODS

We studied 500 patients who were 18 to 80 years of age and who were undergoing elective open colorectal resection, in most cases for cancer or inflammatory bowel disease. We included pa-

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tients who were undergoing abdominal–peritoneal pull-through procedures, but not those scheduled for minor colon surgery (e.g., polypectomy or isolated colostomy). Other exclusion criteria were a recent history of fever, infection, or both; serious malnutrition (as indicated by a serum albumin concentration of less than 3.3 g per deciliter, a white-cell count of less than 2500 cells per cubic millimeter, or the loss of more than 20 percent of body weight); and bowel obstruction. The institutional review board at each of the three participating institutions approved the study, and all patients provided written informed consent.

Study Protocol

The night before surgery, the patients underwent a standard mechanical bowel preparation with an electrolyte solution. Intraluminal antibiotics were not used, but patients in both groups were given prophylactic intravenous antibiotic therapy for a mean (±SD) of 2.7±2.3 days after the skin incision. Most patients were given metronidazole combined with cefazolin, cefamandole, amoxicillin–clavulanate, or mezlocillin.

Anesthesia was induced with thiopental sodium (3 to 5 mg per kilogram of body weight), fentanyl (1 to 3 μg per kilogram), and vecuronium bromide (0.1 mg per kilogram) given intravenously. It was subsequently maintained with isoflurane, the dose of which was adjusted to keep the mean arterial blood pressure within 20 percent of the preinduction value. Additional fentanyl was administered when the surgery was completed to improve analgesia when the patient emerged from anesthesia.

After the induction of anesthesia and endotracheal intubation, each patient was assigned to one of two groups through the use of a set of computer-generated random numbers. The assignments were stratified according to the participating hospital and were kept in sealed, sequentially numbered envelopes until used. One group of patients received 30 percent oxygen and 70 percent nitrogen; the other group received 80 percent oxygen and 20 percent nitrogen.

The intraoperative administration of gas at the assigned concentrations continued until immediately before extubation, when oxygen was increased to 100 percent during extubation. The concentrations were then returned to the previous levels as soon as deemed safe by the anesthesiologist. During the first two hours of recovery, oxygen at the specified concentration was given through a nonrebreathing mask (AirCare, Apotheus Laboratories, Lubbock, Tex.) that was sealed to the patient's face and connected to a valved manifold and oxygen blender. Patients in both treatment groups subsequently breathed ambient air unless additional oxygen was required to maintain an oxyhemoglobin saturation of more than 92 percent.

The anesthesiologists who cared for the patients were aware of their treatment-group assignments. However, cardboard shields were positioned over flowmeters and relevant monitors to prevent the surgical team from determining the fraction of inspired oxygen. Two hours after a patient's recovery from anesthesia, the record of the administration of anesthesia and the blood gas results were sealed so that the surgeons and investigators who evaluated the wounds postoperatively would be unaware of the patients' treatment-group assignments. Patients were not informed of their group assignments.

The patients were aggressively hydrated during and after surgery because hypovolemia decreases perfusion of the wound and increases the incidence of infection.[4] A crystalloid solution was administered intravenously at a rate of 15 ml per kilogram per hour throughout surgery. Blood that had been lost was replaced with a crystalloid solution in a solution-to-blood ratio of 4:1 or a colloid solution in a solution-to-blood ratio of 2:1. Fluids were administered at a rate of 3.5 ml per kilogram per hour for the first 24 hours after surgery and at a rate of 2 ml per kilogram per hour for the subsequent 24 hours. Leukocyte-depleted blood was administered if deemed necessary by the attending surgeon.

There was no antibiotic or antiseptic irrigation of the wound or peritoneal cavity. The technique for wound closure was standardized: all deep layers of the wound, including the peritoneum, were closed with continuous sutures. Subcutaneous tissues were closed with interrupted sutures, and the skin was stapled.

The intraoperative core temperature was maintained at 36°C with the use of a forced-air cover over the patient and warming of intravenous fluid.[15] Postoperative pain was treated with intravenous and intramuscular opioids administered by a nurse who was unaware of the patient's treatment-group assignment. The attending surgeon, who was also unaware of the patient's treatment-group assignment, determined when to restart feeding, when to remove the staples, and when to discharge the patient from the hospital. The timing of discharge was based on routine surgical considerations, including the return of bowel function, the control of any infections, and adequate healing of the incision.

Evaluation

Relevant clinical characteristics of patients in each group were recorded. Preoperative laboratory values and factors that might influence the healing of wounds or resistance to infection were recorded. These included smoking history, preoperative hemoglobin concentration, and any coexisting systemic diseases and drug therapy.

We used two scales to evaluate the risk of infection. The scoring system of the Study on the Efficacy of Nosocomial Infection Control (SENIC) of the Centers for Disease Control and Prevention assigns one point for each of the following factors: three or more underlying diagnoses at discharge, surgery that lasts two or more hours, an abdominal site of surgery, and the presence of a contaminated or infected wound.[1] We modified the system slightly from its original form by using the number of diagnoses at admission rather than at discharge. The National Nosocomial Infection Surveillance System (NNISS) predicts risk on the basis of the type of surgery, the rating of physical status on a scale developed by the American Society of Anesthesiologists (on which a preoperative score of 1 indicates that the patient is healthy and a score of 5 indicates that the patient is critically ill), and the duration of surgery.[16] For both scales, higher scores indicate a greater risk of infection. Scores were determined before surgery and randomization.

Intraoperative core temperatures were measured in the distal esophagus (Mon-a-Therm, Mallinckrodt Anesthesiology Products, St. Louis). Infrared aural-canal temperatures (Exergen, Watertown, Mass.) or axillary temperatures were then recorded daily throughout hospitalization. Detailed records of anesthetic and fluid management (including urine output) were kept. Concentrations of inspired oxygen and end-tidal isoflurane and carbon dioxide were measured during anesthesia. Oxygen saturation was measured with pulse oximeters during anesthesia and throughout recovery. Arterial blood was obtained one hour after the induction of anesthesia and two hours after recovery from anesthesia for the measurement of the partial pressure of oxygen.

Surgical wounds were evaluated daily by physicians who were not members of the surgical team and who were unaware of the treatment-group assignments. Patients were then evaluated by the same investigators at a clinic visit two weeks after surgery. We determined the infection status of patients who did not return to the clinic by calling their physicians.

Wounds were considered likely to be infected when pus could be expressed from the incision or aspirated from a loculated mass within the wound. Pus was cultured, and wounds were considered infected when bacteria were cultured from the pus.[2] Only infections diagnosed within 15 days after surgery were included in our analysis.

The healing and infection of wounds were scored with the ASEPSIS system.[17] The score is derived from the weighted sum of points assigned for the following factors: duration of administration of antibiotics, drainage of pus during local anesthesia, débridement of the wound during general anesthesia, serous discharge, erythema, purulent exudate, separation of deep tissues, isolation of bacteria from the discharge, and hospitalization for more than 14 days. Higher scores indicate poorer healing and a greater likelihood of infection. As an additional indicator of clinical infection, differential white-cell counts were determined preoperatively and on days 1, 3, 6, and 9 after surgery.

In a subgroup of 54 patients at one center (32 of whom were given 30 percent oxygen and 22 of whom were given 80 percent oxygen), we evaluated collagen and protein deposition in wounds.

Near the end of surgery, a 7-cm-long expanded polytetrafluoroethylene implant (Impra, International Polymer Engineering, Tempe, Ariz.) was inserted into the subcutaneous tissue a few centimeters to one side of and parallel to the surgical incision. On the seventh day after surgery, the implant was removed and assayed for hydroxyproline and protein.[18] In the same subgroup, we measured subcutaneous oxygen tension using a sensor of oxygen in tissue (Licox Medical Systems, Greenvale, N.Y.) positioned within a subcutaneous, saline-filled tonometer inserted in the lateral upper arm.[19] Measurements began as soon as practical after the induction of anesthesia and continued at the designated concentration of oxygen throughout surgery and for two hours postoperatively.

In a subgroup of 24 patients (12 per group) at one center, we measured oxygen tension in muscle during surgery. An oxygen electrode was inserted into the quadriceps femoris with a needle 0.35 mm in diameter and driven into the muscle 1 mm at a time.[20] At each of 200 measurement points, tissue oxygen tension was recorded. From these values, a histogram of tissue oxygen tensions was constructed for each patient.[21] Muscle oxygen tension was evaluated 90 minutes after the induction of anesthesia at the designated fraction of inspired oxygen.

Statistical Analysis

We planned to study a maximum of 1000 patients and to evaluate results after a total of 500 or 750 patients were enrolled. The a priori criterion for ending the study after the enrollment of 500 patients was a difference in the incidence of surgical-wound infections between the two groups with a one-tailed P value of less than 0.012. The study would be stopped after the enrollment of 750 patients if the P value for the difference between the groups was less than 0.016. To compensate for the two initial analyses, a P value of 0.036 would be required for significance on completion of the analysis of all 1000 patients. The overall one-tailed risk of a type I error was thus 5 percent.[22]

We used an intention-to-treat analysis.[23] We considered patients to be in the group to which they were assigned (even if the concentration of oxygen was increased to maintain adequate saturation), and the denominator for each group was all patients assigned to that group (including patients who declined follow-up evaluations of wounds). All outcome events were included in our primary comparison.

Repeated measurements, such as those of tissue oxygen concentration, were averaged over time for each patient and then averaged among the patients in each treatment group. The numbers of postoperative wound infections in each group were analyzed with two-tailed chi-square tests. Other results and potential confounding factors were evaluated with two-tailed chi-square tests, unpaired t-tests, or Mann–Whitney U tests, as appropriate. All P values are two sided.

We used multiple logistic-regression analysis to assess the fractional contribution of potentially predictive factors. These included treatment group, study center, sex, age, weight, height, smoking status, physical status as rated on the scale of the American Society of Anesthesiologists, diagnosis, operation site, preoperative hemoglobin concentration and hematocrit, intraoperative use of opioids (fentanyl), postoperative use of opioids (piritramid), intraoperative isoflurane concentration, duration of surgery, and scores on the SENIC and NNISS scales. Factors that had a P value of less than 0.25 on univariate analysis were entered into the mixed-effects model; those that contributed less than 10 percent to the overall ability of the model to predict the incidence of wound infections were sequentially eliminated.

RESULTS

From July 1996 to October 1998, we enrolled 500 patients, 223 (45 percent) at the Donauspital (Vienna, Austria), 213 (43 percent) at the University of Vienna (Vienna, Austria), and 64 (13 percent) at the University Hospital Eppendorf (Hamburg, Germany). Enrollment in the study was discontinued after 500 patients had been enrolled because the incidence of surgical-wound infection in the two groups differed significantly ($P<0.012$). Two-hundred fifty patients had been assigned to each group, and an audit confirmed that the patients were given the assigned treatment. Follow-up evaluations of wounds were not completed in three patients who withdrew from the study. These patients had no known infections, and in our analysis we considered them to be uninfected (Fig. 1).

The types of prophylactic antibiotics used and the duration of their administration were similar in the two groups. The perioperative administration of oxy-

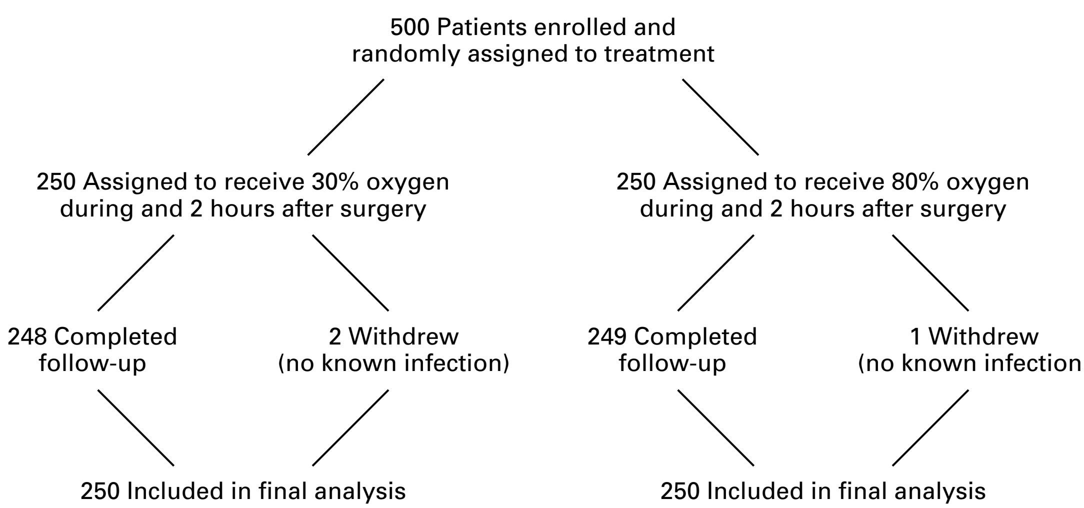

Figure 1. Assignment and Analysis of the 500 Patients in the Study. The patients who withdrew were assumed to be uninfected.

TABLE 1. CHARACTERISTICS OF THE PATIENTS IN THE TWO GROUPS.*

CHARACTERISTIC	PATIENTS WHO RECEIVED 30% OXYGEN (N=250)	PATIENTS WHO RECEIVED 80% OXYGEN (N=250)	P VALUE
Base line			
Sex — M/F	137/113	143/107	0.65
Weight — kg	72±17	74±17	0.26
Height — cm	169±12	170±12	0.45
Age — yr	57±15	57±15	0.80
American Society of Anesthesiologists physical-status score — %			0.60
1 (healthy)	29	22	
2 (minimal illness)	53	63	
3 (moderately ill)	18	15	
Smoker — %	29	24	0.19
Diagnosis — %			0.07
Cancer	55	65	
Inflammatory bowel disease	25	20	
Other	20	15	
Operative site — %			0.12
Colon	63	71	
Rectum	37	29	
Hemoglobin — g/dl	13±2.1	12.8±2.1	0.25
Intraoperative			
Dose of fentanyl — mg	0.84±0.47	0.76±0.42	0.07
End-tidal isoflurane concentration — %	0.84±0.24	0.90±0.24	0.005
Mean arterial pressure — mm Hg	88±11	89±10	0.25
Heart rate — beats/min	78±13	75±11	0.35
Crystalloid infusion — liters	4.2±1.9	3.9±1.7	0.16
Colloid infusion			
No. of patients (%)	166 (66)	162 (65)	0.81
Volume — liters	0.8±0.6	0.8±0.6	0.34
Red-cell transfusion			
Patients — no. (%)	71 (28)	78 (31)	0.56
Units of red cells	3.1±3.9	3.0±2.1	0.83
Duration of surgery — hr	3.1±1.4	3.1±1.4	0.94
Core temperature — °C	36.0±0.6	35.9±0.5	0.09
Arterial oxygen saturation — %	98.7±1.1	99.7±0.6	<0.001
Subcutaneous oxygen tension — mm Hg†	59±15	109±43	<0.001
Muscle oxygen tension — mm Hg‡	25±6	49±10	<0.001
Partial pressure of arterial oxygen — mm Hg	121±34	348±97	<0.001
Postoperative			
Duration of prophylactic antibiotics — days	2.7±2.3	2.7±2.3	0.99
Hemoglobin — g/dl	11.5±1.6	11.5±1.6	0.99
Dose of piritramid — mg	10.0±4.9	10.4±5.1	0.42
Oxygen saturation on pulse oximetry — %	97±2	99±2	<0.001
Subcutaneous oxygen tension — mm Hg†	54±25	73±25	0.02
Partial pressure of arterial oxygen — mm Hg	114±35	206±91	<0.001
SENIC score — no. of patients§			0.80
1	65	71	
2	165	158	
3	20	21	
NNISS score — no. of patients¶			0.86
0	127	132	
1	106	100	
2	17	18	
Infection rate predicted by NNISS — %	6.3	6.2	

*Plus–minus values are means ±SD. All P values are two-tailed. SENIC denotes Study on the Efficacy of Nosocomial Infection Control,[1] and NNISS National Nosocomial Infection Surveillance System.[16]

†Subcutaneous oxygen tension was measured in 32 patients who received 30 percent oxygen and 22 patients who received 80 percent oxygen.

‡Muscle oxygen tension was measured in 12 patients who received 30 percent oxygen and 12 patients who received 80 percent oxygen.

§The rates of surgical-wound infection reported in SENIC were 3.6 percent, 8.9 percent, and 17.2 percent with scores of 1, 2, and 3, respectively.[1] Higher scores indicate a greater risk of infection.

¶The rates of surgical-wound infection reported in NNISS for colon resection were 3.2 percent, 8.5 percent, and 16.1 percent with scores of 0, 1, and 2, respectively.[16] Higher scores indicate a greater risk of infection.

gen in concentrations that exceeded those designated was required in 38 patients assigned to receive 30 percent oxygen, but in only 1 assigned to receive 80 percent oxygen. Most patients returned for the follow-up visit two weeks after surgery; no previously unidentified wound infections were detected in the clinic or by telephone consultation with the patients' physicians.

The clinical characteristics, diagnoses, surgical procedures, duration of surgery, hemodynamic values, and use of anesthetics were similar in the two groups of patients (Table 1). The patients who received 80 percent oxygen were given slightly more isoflurane than the patients who received 30 percent oxygen (mean [±SD] end-tidal concentration, 0.90±0.24 percent vs. 0.84±0.24 percent), a difference that was not clinically important.

Arterial oxygen saturation and partial pressure of arterial oxygen were significantly higher intraoperatively in the patients who received 80 percent oxygen. Subcutaneous oxygen tension was significantly higher during and after surgery in the patients who received 80 percent oxygen. Intraoperative oxygen tension in muscle was also significantly higher in the patients given 80 percent oxygen (Table 1).

The overall incidence of surgical-wound infections was 8 percent, which was only slightly higher than the 6 percent predicted by the score on the NNISS scale. Although the scores for the risk of infection on the SENIC and NNISS scales were similar in the two groups (Table 1), surgical-wound infections occurred in only 13 patients who received 80 percent oxygen (5.2 percent; 95 percent confidence interval, 2.4 to 8.0 percent), as compared with 28 patients given 30 percent oxygen (11.2 percent; 95 percent confidence interval, 7.3 to 15.1 percent; P=0.01). The absolute difference in the rates of infection in the two groups was thus 6.0 percent (95 percent confidence interval, 1.2 to 10.8 percent).

Most positive cultures contained several organisms: the important ones were *Escherichia coli* (17 patients), enterococcus (9 patients), *Pseudomonas aeruginosa* (8 patients), *Staphylococcus aureus* (2 patients), *S. epidermidis* (2 patients), and enterobacter (2 patients). Culture-negative pus was expressed from the wounds of six patients given 30 percent oxygen and four given 80 percent oxygen. The mean ASEPSIS wound scores were higher in patients given 30 percent oxygen than in patients given 80 percent oxygen (5±9 vs. 3±7, P=0.01). The infection rates at the three hospitals did not differ significantly.

Twelve patients in the group that received 30 percent oxygen (4.8 percent) and five in the group that received 80 percent oxygen (2.0 percent) required admission to the intensive care unit (P=0.14). Most admissions were for surgical complications, including dehiscence, anastomotic leak, and peritonitis. Six patients in the group that received 30 percent oxygen (2.4 percent) and one in the group that received 80 percent oxygen (0.4 percent) died within 15 days after surgery (P=0.13). The cause of death in most patients was sepsis and multiorgan failure. The extent of collagen deposition and protein deposition, time to first solid food and suture removal, and duration of hospitalization were similar in the two groups (Table 2). Only the use of 30 percent oxygen correlated significantly with the risk of infection in the mixed-effects model, with an odds ratio of 2.3 (95 percent confidence interval, 1.2 to 4.6).

Patients with infection had significantly higher ASEPSIS scores and postoperative white-cell counts. Patients with infection had their staples removed one day later after surgery than patients with no infection (P<0.001), and the duration of hospitalization was prolonged by a week (P<0.001) (Table 3). There

TABLE 2. Outcomes in the Two Study Groups.*

Characteristic	Patients Who Received 30% Oxygen (N=250)	Patients Who Received 80% Oxygen (N=250)	P Value
Infection — no. (%)	28 (11.2)	13 (5.2)	0.01
ASEPSIS score†	5±9	3±7	0.01
Collagen deposition — ng/mm‡	267±109	258±118	0.38
Protein deposition — μg/mm‡	163±74	153±91	0.31
First solid food — days after surgery	4.4±1.6	4.5±1.8	0.27
Staples removed — days after surgery	10.4±1.5	10.3±1.4	0.21
Duration of hospitalization after surgery — days	11.9±4.0	12.2±6.1	0.26

*Plus–minus values are means ±SD. All P values are two-tailed.

†Higher scores indicate poorer healing and a greater likelihood of infection.

‡Collagen deposition and protein deposition were measured in 32 patients who received 30 percent oxygen and 22 patients who received 80 percent oxygen.

TABLE 3. Outcome According to the Presence or Absence of Wound Infection.*

Characteristic	Infection (N=41)	No Infection (N=459)	P Value
ASEPSIS score†	25±13	2±4	<0.001
White-cell count ($\times 10^{-3}$/mm^3)			
Before surgery	8.1±3.0	7.5±2.8	0.19
First day after surgery	11.5±4.0	10.1±3.4	0.02
Third day after surgery	10.7±3.1	8.7±3.2	0.001
Sixth day after surgery	12.5±3.5	8.4±3.2	<0.001
Ninth day after surgery	11.7±4.9	9.0±3.5	0.003
Staples removed (days after surgery)	11.1±2.4	10.3±1.4	<0.001
Duration of hospitalization (days)	18.7±8.3	11.4±4.1	<0.001

*Plus–minus values are means ±SD. All P values are two-tailed.

†Higher scores indicate poorer healing and a greater likelihood of infection.

was no significant difference in the infection rate between smokers and nonsmokers.

DISCUSSION

The administration of supplemental oxygen during colorectal resection and for two hours afterward reduced the incidence of wound infection — one of the most serious common complications of surgery — by half.

Surgical-wound infections are expensive.[24,25] For example, postoperative infections in patients with cancer add an average of $12,500 per patient to the cost of care.[26] One study estimated that 0.5 percent of hospital costs can be attributed to wound infections.[27] The one-week-longer hospitalization in patients with infection in our study is consistent with findings in previous studies[2,28] and indicates that the infections were clinically important, as do the higher numbers of admissions to the intensive care unit and of deaths in the group given 30 percent oxygen.

We used a sealed mask and a manifold system to deliver oxygen postoperatively so that the administration of oxygen could be controlled precisely. However, similar amounts of oxygen can be delivered through conventional nonrebreathing masks. The postoperative administration of oxygen through a conventional mask introduces little if any extra cost, because virtually all patients are given some oxygen after surgery. A previously reported subgroup analysis of 30 patients revealed that supplemental oxygen did not worsen pulmonary function or cause atelectasis, as indicated by chest radiographs or computed tomographic scans.[29] Another subgroup analysis of 231 patients revealed that supplemental oxygen halved the incidence of postoperative nausea and vomiting.[30]

The formation of scars requires hydroxylation of proline and lysine residues.[31] The prolyl and lysyl hydroxylases that catalyze this reaction require oxygen as a substrate.[31] However, the Michaelis–Menten constant for oxygen of prolyl hydroxylase is 20 to 25 mm Hg.[32,33] Proline hydroxylation of collagen will thus be relatively insensitive to the partial pressure of oxygen in the measured range of values for subcutaneous oxygen tension. That the extent of collagen deposition (scar formation) and the time to staple removal were similar in our two study groups is consistent with this theory and suggests that healing in the absence of infection was not improved by supplemental oxygen.

As might be expected from the similar rates of healing, the duration of hospitalization was similar in the two groups. This finding contrasts with the results of our previous study, in which patients were allowed to become mildly hypothermic during surgery.[2] The patients who became hypothermic had a higher incidence of infection and delayed hospital discharge. However, they also had poor healing because hypothermia reduced the amount of collagen deposition and delayed the removal of sutures, even in patients with no infection. These conditions suggest that factors other than infection, such as healing itself, affected the timing of discharge.

We[2] and others[34,35] have identified smoking as a significant risk factor for surgical-wound infection. We were thus surprised that no similar correlation was evident in our current study. However, an important difference between this and previous studies is that smoking is no longer allowed in patients' rooms; furthermore, smoking areas are not even readily accessible from some wards.

In summary, the administration of supplemental oxygen during colorectal resection and for two hours afterward halved the incidence of surgical-wound infection. Because the cost of and risk associated with supplemental perioperative oxygen are trivial, the provision of supplemental oxygen appears to be a practical method of reducing the incidence of this dangerous and expensive complication.

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APPENDIX

The following investigators participated in the study: Donauspital, Vienna, Austria — W. Feil, L. Koller, S. Laciny, J. Neumark, F. Niedermayer, B. Rapf, S. Seisenbacher, T. Wasinger; Vienna General Hospital, University of Vienna, Vienna, Austria — L. Akça, W. Erlacher, R. Fugger, V. Goll, F. Herbst, H. Hetz, C. Hieber, M. Imhof, F.X. Lackner, K. Lampl, R. Lenhardt, E. Marker, P. Nagele, O. Panzer, B. Petschnigg, O. Plattner, S. Roka, A. Schoellkopf, A.M. Schultz, F. Seibt, T. Wallner, J. Wang, A. Werba, K.H. Wiesenger, J. Zacherl, M. Zimpfer; University Hospital Eppendorf, Hamburg, Germany — M. Burmeister, G. Redmann, J. Schulte am Esch, T. Standl; University of California–San Francisco, San Francisco — H. Hopf, H. Scheuenstuhl, F. Tayefeh; Washington University, St. Louis — Ç.F. Arkiliç.

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