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High-concentration supplemental perioperative oxygen and surgical site infection following elective colorectal surgery for rectal cancer: a prospective, randomized, double-blind, controlled, single-site trial

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Abstract

BACKGROUND: Perioperative supplemental oxygen has been proposed to decrease the incidence of surgical site infection (SSI) in colorectal surgery with controversial results. We have assessed the influence of hyperoxygenation on SSI by using the most homogeneous study population.

METHODS: We studied, in a prospective randomized study, 81 patients, who underwent elective open infraperitoneal anastomosis for rectal cancer. Patients were assigned randomly to an oxygen/air mixture with a fraction of inspired oxygen (FiO_2) of 30% ($n = 41$) or 80% ($n = 40$). Administration was commenced after induction of anesthesia and maintained for 6 hours after surgery.

RESULTS: The overall wound infection rate was 21%: 11 patients (26.8%) had wound infections in the 30% FiO_2 group and 6 (15%) in the 80% FiO_2 group ($P < .05$). The risk of SSI was 41% lower in the 80% FiO_2 group.

CONCLUSION: Supplemental 80% FiO_2 reduced postoperative SSI with few risks to the patient and little associated cost.

Colorectal operations are, at best, clean–contaminated procedures, and at times there is contamination of both the peritoneal cavity and the surfaces of the surgical wound. In addition, the diseases of the large bowel that require surgery tend to afflict elderly patients. Collectively, the combination of an unclean environment, major surgery, and debilitated patients creates a situation that is associated with a very high incidence of wound infection. In open colorectal surgery, the incidence of surgical site infection (SSI) varies from 2% to 25% and is associated with a body mass index (BMI) of greater than or equal to 30, creation/revision/reversal of an ostomy, perioperative transfusion, male sex, and an American Society of Anesthesiologists (ASA) score greater than or equal to 3.[1] The incisional SSI

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rates in colon (n = 339) and rectal (n = 217) resections were 9.4% and 18% (P = .0033), respectively. Risk factors for SSI in colon surgery were ostomy closure (odds ratio [OR] = 7.3) and lack of oral antibiotics (OR = 3.3), while in rectal surgery, risk factors were perioperative steroids (OR = 3.7), preoperative radiation (OR = 2.8), and ostomy creation (OR = 4.9).[2] Several interventions have been investigated as part of an evidence-based approach to reduce SSIs: the use, timing, route, and dosing of prophylactic antibiotics[3]; the use of WBC-depleted RBC transfusions[4]; the avoidance of hair shaving[5]; the prevention of intraoperative hypothermia[6]; and the use of mechanical bowel preparation.[7] Despite these measures, significant clinical and economic burden of SSIs persists.[8]

The use of supplemental perioperative oxygen has also been investigated, specifically in elective colorectal surgery patients, with conflicting reports in regard to its effectiveness in reducing SSIs.[9–12]

One of the principal reasons for such mixed results may be that prior trials have entered a heterogeneous population of patients and procedures, which may have precluded the discovery of small but important differences. To overcome this problem, we performed a prospective, randomized, controlled trial in a patient population with a single diagnosis (extraperitoneal rectal cancer), using one surgical standard approach (open colorectal resection through a midline laparotomy). Hence, the aim of our study was to obtain satisfactory statistical information considering the effects of hyperoxygenation on SSI following this procedure in a relatively homogeneous study population.

Materials and Methods

From February 2008 to 2013, we studied, in a prospective randomized study, 81 patients consecutively (45 men, 36 women; mean age 69.8 years), who underwent elective open colorectal resection for middle or low rectal cancer (extraperitoneal rectal cancer). Exclusion criteria included expected surgery time of less than 1 hour, fever or existing signs of infection, diabetes mellitus (type 1 or 2), known immunologic dysfunction (advanced liver disease, HIV infection, hepatitis C virus infection), weight loss exceeding 20% in the previous 3 months, serum albumin concentration of less than 30 g/L, and a leukocyte count of less than 2,500 cells/mL. During hospitalization, the patients were not given antispastic drugs, steroids, or nonsteroidal anti-inflammatory drugs, apart from nonsteroidal anti-inflammatory drugs delivered IV (ketorolac tromethamine). Medical history was recorded, and a systematic physical examination was performed preoperatively. Patients were considered to have respiratory disease when they had a history of chronic obstructive pulmonary disease, asthma requiring routine medication, or other clinically important respiratory impairment. The patients were classified as grade I, II, or III, according to the ASA grading system.

The risk of infection was assessed with the NNISS (National Nosocomial Infections Surveillance System) and the SENIC (Study on the Efficacy of Nosocomial Infection Control) scales.[13,14] The NNISS and SENIC scores have been extensively validated, and larger values with these scores indicate a greater risk of infection.

In the SENIC scoring system,[14] 1 point is given for each of the following:

- presence of 3 or more diagnosis;
- surgery lasting longer than 2 hours;
- operation classified as contaminated or dirty-infected;
- abdominal surgery.

In the NNISS scoring system,[13] 1 point is given for each of the following:

- ASA score of 3, 4, or 5;
- operation classified as contaminated or dirty-infected;
- operation lasting longer than expected for the operative procedure being performed.

Mechanical bowel preparation was not performed. One hour before surgery, prophylactic antibiotics were administered (ceftriaxone 2 g i.v. and metronidazole 500 mg i.v.) followed postoperatively by 2 doses of metronidazole (500 mg i.v.). Prophylactic subcutaneous heparin was administered and given daily until discharge from the hospital. Anesthesia was obtained using the same procedure across all patients. Preanesthesia was accomplished using atropine (.01 mg/kg) plus promethazine (.5 mg/kg) induction using sodium thiopental (5 mg/kg) and atracurium (.5 mg/kg), and tracheal intubation and assisted ventilation using nitrogen dioxide (NO_2)/oxygen (O_2) in the ratio 2:1. After intubation, anesthesia was maintained with oxygen in air, sevoflurane, and remifentanil (.25 µg/kg/minute).

After induction of anesthesia and endotracheal intubation, the patients were assigned randomly to an oxygen/air mixture with a fraction of inspired oxygen (FiO_2) of 30% (Group 1) or 80% (Group 2).

Patients were not informed of their group assignments. Also, the surgical team was blinded to the oxygen concentration administered.

The Ethical Committee of the University of L'Aquila approved the study protocol. All patients gave informed written consent.

The surgical technique consisted of a midline laparotomy. Division of the rectum was carried out with a linear endoscopic 45-mm Roticulator stapler. Proximal section of the vascular arcade was performed, avoiding problems of tension or blood supply. The anastomosis was fashioned with a mechanical circular stapler, usually 31 mm and occasionally 29 mm in diameter, according to the double-stapled technique (end-to-end transanal colorectal anastomosis). When the distal clearance of the inferior margin of the tumor was at the level of the surgical anal canal, or in a narrow pelvis where a transverse stapled section was sometimes impossible, the technique of choice was to perform a rectal mucosectomy and a true coloanal