Oxygen
-
What Does It Have To Do With Surgical Site Infection?

E. Patchen Dellinger, MD, FACS
University of Washington
Caring for the Critically Ill Patient

ABC = airway, breathing, circulation
Preventing Surgical Site Infections (SSI)

ABC = airway, breathing, circulation
= temperature, oxygen, fluids

ABCD - Add drugs (antibiotics)

Add - glucose control
surgical technique
teamwork
other ??
Oxygen and SSI
Influence of Oxygen on the Development of Wound Infection

Diameter Infectious Necrosis (mm)

Hours After Innoculation

Oxygen and Neutrophil Killing

Per Cent Killing, S. aureus

\( pO_2 \)

“…neutrophils have no way of knowing what type of operation we have performed…”

Lee, Infect Dis News 15: 35-37, 2002
Oxygen and Bacterial Growth in Wound

Days after inoculation of $10^6$ Pseudomonas

Soft Tissue Oxygenation

Excellent perfusion

Vasoconstriction
Anemia and Tissue Oxygen Tension

- Experimental subjects rendered acutely anemic with simultaneous volume replacement and temperature control
- Hgb 12.8 reduced to 5.0
- No significant change in tissue pO₂
Wound Oxygen Tension & SSI

Observed-Expected SSI Rate

Maximum wound $\text{pO}_2$

Near InfraRed O2 Saturation in the Surgical Incision at 12 hrs after Vascular Surgery

Arm Tissue $O_2$ Saturation and SSI

Govinda. Anesth & Analg 2010; 111: 946-52
Oxygen and SSI

• Oxygen tension in the wound is important.

• How to translate that into clinical practice that lowers SSI is less obvious.
Oxygen in the Wound

It’s **not** the same as arterial oxygen tension

It is affected by:

- $\text{FiO}_2$
- Cardiac output
- Regional vs General anesthesia
- Pain management
- Fluid management
- Temperature
- Other ?
Temperature and SSI
(Oxygen)
Temperature and Tissue $O_2$ tension

- Subcut temp increase 4° C
- Subcut $O_2$ tension increase 40 torr
- Linear correlation between temperature and $O_2$ tension
- Threefold increase in local perfusion

Rabkin. Arch Surg 1987;122:221
Temperature and SSI Following Colectomy

• Mechanical bowel prep
• Parenteral antibiotics at induction x 4 d
• Standard anesthetic-isoflurane
• Randomized after induction
  \( T \geq 36.5 \degree \text{C} \) or \( T \geq 34.5 \degree \text{C} \)
• Supplemental O\(_2\) in PACU x 3h
• Aggressive fluid resuscitation

Kurz. NEJM 1996;334:1209
Temperature and SSI Following Colectomy

<table>
<thead>
<tr>
<th></th>
<th>Normo (104)</th>
<th>Hypo (96)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSI</td>
<td>6</td>
<td>18</td>
<td>.009</td>
</tr>
</tbody>
</table>

Kurz. NEJM 1996;334:1209
Temperature and SSI Following Cholecystectomy

Hypothermia on arrival in PACU

<table>
<thead>
<tr>
<th></th>
<th>T&lt;36</th>
<th>T≥36</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>156</td>
<td>105</td>
<td></td>
</tr>
<tr>
<td>SSI</td>
<td>18 (12%)</td>
<td>2 (2%)</td>
<td>0.004</td>
</tr>
</tbody>
</table>

Flores-Maldonado. Arch Medical Research 2001; 32: 227-31
Local Warming and SSI after Clean Operations

• Elective hernia repair
• Varicose vein operation
• Breast operation, incision ≥ 3cm
• Pre-op warming ≥ 30 min
  Whole body forced air - systemic
  Incision site radiant heat - local

Melling. Lancet 2001;358:876
Local Warming and SSI after Clean Operations

<table>
<thead>
<tr>
<th></th>
<th>Local</th>
<th>Systemic</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSI*</td>
<td>5 (4%)</td>
<td>8 (6%)</td>
<td>19 (14%)</td>
</tr>
<tr>
<td>Post-op antibiotics*</td>
<td>9 (7%)</td>
<td>9 (7%)</td>
<td>22 (16%)</td>
</tr>
</tbody>
</table>

* p < 0.01

Melling. Lancet 2001;358:876
Perioperative Warming, Intraoperative Temperature and Complications

- Open abdominal operation with bowel resection
- All patients warmed in the O.R.
- Study group (perioperative) warmed 2 hours preop and 2 hours postop

Perioperative Warming, Intraoperative Temperature and Complications

<table>
<thead>
<tr>
<th></th>
<th>Periop N=47</th>
<th>Standard N=56</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood loss</td>
<td>200 ml</td>
<td>400 ml</td>
<td>0.011</td>
</tr>
<tr>
<td>Any complication</td>
<td>32%</td>
<td>54%</td>
<td>0.027</td>
</tr>
<tr>
<td>SSI</td>
<td>13%</td>
<td>33%</td>
<td>0.09</td>
</tr>
</tbody>
</table>

Hypothermia During Anesthesia

Squared Core Temp (°C)

Elapsed Time (h)
Redistribution Hypothermia

Vasoconstricted ➔ Anesthesia ➔ Vasodilated

Core 37°C
Periphery 31-35°C

Core 36°C
Periphery 33-35°C
Keeping Your Patient Warm in the O.R.

- Prewarming and active warming in the O.R. is much more important than the O.R. room temperature.

- If you raise O.R. room temperature from $20^\circ$ to $27^\circ$, you still have an $10^\circ$ gradient between the patient’s temperature and the room temperature and everyone in the room is miserable.
<table>
<thead>
<tr>
<th>Temperature Range</th>
<th>Count/Total</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 36°C</td>
<td>7836/8132</td>
<td>(96.4%)</td>
</tr>
<tr>
<td>&gt; 36°C &amp; &lt; 36.5°C</td>
<td>1047/2647</td>
<td>(40%)</td>
</tr>
<tr>
<td>&gt; 36.5°C</td>
<td>1491/2647</td>
<td>(56%)</td>
</tr>
</tbody>
</table>
Oxygen ($\text{FiO}_2$) and SSI
FiO$_2$ and SSI Following Colectomy

Mechanical bowel prep
Parenteral antibiotics x 2.7 + 2.3 d
Standard anesthetic-isoflurane
Randomized after induction
  30% or 80% FiO$_2$ - OR + PACU x 2 h
Temperature $\geq$ 36$^\circ$
Aggressive fluid resuscitation

Greif. NEJM 2000;342:161
**FiO₂ and SSI Following Colectomy**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>30% (250)</th>
<th>80% (250)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SaO₂</td>
<td>99%</td>
<td>100%</td>
</tr>
<tr>
<td>PaO₂</td>
<td>121</td>
<td>348</td>
</tr>
<tr>
<td>PO₂ - S.C.</td>
<td>59</td>
<td>109</td>
</tr>
<tr>
<td>PO₂ - muscle</td>
<td>25</td>
<td>49</td>
</tr>
</tbody>
</table>

Greif. NEJM 2000;342:161
FiO$_2$ and SSI Following Colectomy

<table>
<thead>
<tr>
<th></th>
<th>30% (250)</th>
<th>80% (250)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSI</td>
<td>28 (11.2%)</td>
<td>13 (5.2%)</td>
</tr>
<tr>
<td>Collagen synth.</td>
<td>equal</td>
<td>equal</td>
</tr>
<tr>
<td>Time to eat</td>
<td>4.4d</td>
<td>4.5d</td>
</tr>
<tr>
<td>Atelectasis (CXR, CT)</td>
<td>equal</td>
<td>equal</td>
</tr>
<tr>
<td>Nausea</td>
<td>---</td>
<td>decreased</td>
</tr>
</tbody>
</table>

Greif. NEJM 2000;342:161
FiO₂ and SSI Following Major Intra-abdominal Procedures

Bowel prep not specified
Parenteral antibiotics
Anesthetic not standardized
Randomized after induction
35% or 80% FiO₂ - OR + PACU x 2 h
Temperature control not described
Fluid resuscitation not standardized

Pryor. JAMA 2004;291:79
# FiO₂ and SSI Following Major Intra-abdominal Procedures

<table>
<thead>
<tr>
<th></th>
<th>FiO₂ 35% (80)</th>
<th>FiO₂ 80% (80)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSI</td>
<td>9 (11.3%)</td>
<td>20 (25%)</td>
</tr>
<tr>
<td>Collagen synth.</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Time to eat</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Atelectasis (CXR, CT)</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Nausea</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Oxygen tension measurements</td>
<td>?</td>
<td>?</td>
</tr>
</tbody>
</table>

Pryor. JAMA 2004;291:79
FiO$_2$ and SSI Following Major Intra-abdominal Procedures

80% Group

Higher BMI  $p = .04$

Twice as many obese pts  $p = .04$

Duration of operation longer  $p = .07$

More blood loss  $p = .03$

++++

Infection surveillance by chart review

Pryor. JAMA 2004;291:79
FiO$_2$ and SSI Following Colectomy

Mechanical bowel prep
Parenteral antibiotics x 48 h
Standard anesthetic
Randomized after induction
  30% or 80% FiO$_2$ - OR + PACU x 6 h
Normothermia maintained
Aggressive fluid resuscitation
Pain management standardized

Belda. JAMA 2005; 294: 2035
FiO$_2$ and SSI Following Colectomy

<table>
<thead>
<tr>
<th>FiO$_2$</th>
<th>30% (143)</th>
<th>80% (148)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSI</td>
<td>35 (24.4%)</td>
<td>22 (14.9%)</td>
</tr>
</tbody>
</table>

Belda. JAMA 2005; 294: 2035
FiO2 and SSI
Three Studies

O₂ and N₂O and SSI?

General Surgery cases randomized to

80% O₂ + 20% N₂ (997 patients)

30% O₂ + 70% N₂O (1015 patients)

Myles. Anesthesiology 2007; 107: 221-31
O₂ and N₂O and SSI?

Myles. Anesthesiology 2007; 107: 221-31
Intraoperative Fraction of Inspired Oxygen Is a Modifiable Risk Factor for Surgical Site Infection after Spinal Surgery


Background: Surgical site infections (SSI) after spinal surgery increase morbidity, mortality, length of hospital stay, and costs. Most previously identified risk factors for these infections, such as severity of illness and procedure duration, are not amenable to intervention. This study sought to identify modifiable risk factors associated with SSI after spinal surgery.

Methods: This is a case-control study including case identification and review of medical records. A total of 104 patients with SSI after spinal surgery were compared to 104 randomly selected control patients without SSI after spinal surgery in a 926-bed tertiary care hospital in Baltimore, Maryland, between April 1, 2001 and December 31, 2004.

Results: Multivariate analysis identified independent risk factors for SSI after spinal surgery including prolonged procedure duration (odds ratio [OR], 4.7; 95% confidence interval [95% CI], 1.6–14; P < 0.001), American Society of Anesthesiologists score of 3 or greater (OR, 9.7; 95% CI, 3.7–25; P < 0.001), lumbar-sacral operative level (OR, 2.9; 95% CI, 1.2–7.1; P = 0.02), posterior approach (OR, 3.5; 95% CI, 1.2–9.7; P = 0.02), instrumentation (OR, 2.5; 95% CI, 1.1–6.0; P = 0.03), obesity (OR, 2.8; 95% CI, 1.0–8.0; P = 0.05), and duration of surgery, likely to die and 60% more likely to spend time in the intensive care unit.2 The Centers for Disease Control and Prevention (CDC) National Healthcare Safety Network (formerly the National Nosocomial Infection Surveillance system) reports rates of between 0.72 and 4.1 SSI per 100 laminectomy or spinal fusion procedures.5 SSI after laminectomy or spinal fusion has been found to prolong total hospital stay by a median of 2 weeks per patient and increase healthcare costs more than 300%.6 These infections can lead to significant morbidity, readmission to the hospital, and additional surgeries, sometimes requiring the removal of implanted spinal hardware.7–9

The National Healthcare Safety Network risk index, a composite score calculated from the American Society of Anesthesiologists (ASA) score, duration of surgery, and wound class, is predictive of SSI for a variety of surgeries, including laminectomy and spinal fusion.10 However, com-
### Spinal Surgery, FiO$_2$, & SSI Multivariate Analysis

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Odds Ratio</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration &gt;75%ile</td>
<td>4.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ASA &gt; 3</td>
<td>9.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lumbo-sacral level</td>
<td>2.9</td>
<td>0.02</td>
</tr>
<tr>
<td>Posterior approach</td>
<td>3.5</td>
<td>0.02</td>
</tr>
<tr>
<td>Instrumentation</td>
<td>2.5</td>
<td>0.03</td>
</tr>
<tr>
<td>Obesity</td>
<td>4.0</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Razor shaving</td>
<td>3.6</td>
<td>0.02</td>
</tr>
<tr>
<td>FiO$_2$ &lt;50%</td>
<td>12</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Perioperative Supplemental Oxygen Therapy and Surgical Site Infection

A Meta-analysis of Randomized Controlled Trials

Motaz Qadan, MBChB, MRCS(Edin); Ozan Akça, MD; Suhal S. Mahid, MRCS, PhD; Carlton A. Hornung, MPH, PhD; Hiram C. Polk Jr, MD

Objective: To conduct a meta-analysis of randomized controlled trials in which high inspired oxygen concentrations were compared with standard concentrations to assess the effect on the development of surgical site infections (SSIs).

Data Sources: A systematic literature search was conducted using the MEDLINE, EMBASE, and Cochrane databases and included a manual search of references of original articles, poster presentations, and abstracts from major meetings (“gray” literature).

Study Selection: Twenty-one of 2167 articles met the inclusion criteria. Of these, 5 randomized controlled trials (3001 patients) assessed the effect of perioperative supplemental oxygen use on the SSI rate. Studies used a treatment-inspired oxygen concentration of 80%. Maximum follow-up was 30 days.

Data Extraction: Data were abstracted by 3 independent reviewers using a standardized data collection form.

Relative risks were reported using a fixed-effects model. Results were subjected to publication bias testing and sensitivity analyses.

Data Synthesis: Infection rates were 12.0% in the control group and 9.0% in the hyperoxic group, with relative risk reduction of 25.3% (95% confidence interval [CI], 8.1%-40.1%) and absolute risk reduction of 3.0% (1.1%-5.3%). The overall risk ratio was 0.742 (95% CI, 0.599-0.919; P = .006). The benefit from increasing oxygen concentration was greater in colorectal-specific procedures, with a risk ratio of 0.556 (95% CI, 0.383-0.808; P = .002).

Conclusions: Perioperative supplemental oxygen therapy exerts a significant beneficial effect in the prevention of SSIs. We recommend its use along with maintenance of normothermia, meticulous glycemic control, and preservation of intravascular volume perioperatively in the prevention of SSIs.

Figure 2. Effect of perioperative supplemental oxygen therapy on surgical site infection risk reduction. Risk ratios (RRs) with 95% confidence intervals (CIs) are shown for individual, combined, and sensitivity analysis (SA) values. 1
Effect of High Perioperative Oxygen Fraction on Surgical Site Infection and Pulmonary Complications After Abdominal Surgery

The PROXI Randomized Clinical Trial

Christian S. Meyhoff, MD, PhD
Jørn Wetterlev, MD, PhD
Lars N. Jorgensen, MD, DMSc
Steen W. Hønneberg, MD, DMSc
Claus Høg dall, MD, DMSc
Lene Lundvall, MD
Poul-Erik Svedsen, MD
Hannah Mollerup, MD
Troels H. Lunn, MD
Inger Simonsen, MD
Kristian R. Martinsen, MD
Therese Pulsawka, MD
Lars Bundgaard, MD
Lasse Bugge, MD
Egon G. Hansen, MD
Claus Riber, MD
Peter Gocht-Jensen, MD
Line R. Walker, MD
Asger Bendtsen, MD
Gun Johansson, MD
Nina Skovgaard, MD
Kim Helto, MD
Andrei Poukinski, MD
André Korshin, MD
Aqil Walli, MD
Mustafa Bulut, MD
Riha S. Cukras, MD, DMSc

Context  Use of 80% oxygen during surgery has been suggested to reduce the risk of surgical wound infections, but this effect has not been consistently identified. The effect of 80% oxygen on pulmonary complications has not been well defined.

Objective  To assess whether use of 80% oxygen reduces the frequency of surgical site infection without increasing the frequency of pulmonary complications in patients undergoing abdominal surgery.

Design, Setting, and Patients  The PROXI trial, a patient- and observer-blinded randomized clinical trial conducted in 14 Danish hospitals between October 2006 and October 2008 among 1400 patients undergoing acute or elective laparotomy.

Interventions  Patients were randomly assigned to receive either 80% or 30% oxygen during and for 2 hours after surgery.

Main Outcome Measures  Surgical site infection within 14 days, defined according to the Centers for Disease Control and Prevention. Secondary outcomes included atelectasis, pneumonia, respiratory failure, and mortality.

Results  Surgical site infection occurred in 131 of 685 patients (19.1%) assigned to receive 80% oxygen vs 141 of 701 (20.1%) assigned to receive 30% oxygen (odds ratio [OR], 0.94; 95% confidence interval [CI], 0.72-1.22; P = .64). Atelectasis occurred in 54 of 685 patients (7.9%) assigned to receive 80% oxygen vs 50 of 701 (7.1%) assigned to receive 30% oxygen (OR, 1.11; 95% CI, 0.75-1.66; P = .60), pneumonia in 41 (6.0%) vs 44 (6.3%) (OR, 0.95; 95% CI, 0.61-1.48; P = .82), respiratory failure in 38 (5.5%) vs 31 (4.4%) (OR, 1.27; 95% CI, 0.78-2.07; P = .34), and mortality within 30 days in 30 (4.4%) vs 20 (2.9%) (OR, 1.56; 95% CI, 0.88-2.77; P = .13).

Conclusion  Administration of 80% oxygen compared with 30% oxygen did not result in a difference in risk of surgical site infection after abdominal surgery.

Trial Registration  clinicaltrials.gov Identifier: NCT00364741

JAMA. 2009;302(14):1543-1550

www.jama.com
**FiO₂, SSI, Atelectasis, & Respiratory Failure**

**PROXI Trial**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>80% FiO₂ N=685</th>
<th>30% FiO₂ N=701</th>
<th>Adjusted Odds Ratio</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSI</td>
<td>131 (19.1%)</td>
<td>141 (20.1%)</td>
<td>0.91</td>
<td>0.69 – 1.20</td>
</tr>
<tr>
<td>Atelectasis</td>
<td>54 (7.9%)</td>
<td>50 (7.1%)</td>
<td>1.13</td>
<td>0.75 – 1.72</td>
</tr>
<tr>
<td>Resp Failure</td>
<td>38 (5.5%)</td>
<td>31 (4.4%)</td>
<td>1.22</td>
<td>0.74 – 2.03</td>
</tr>
</tbody>
</table>

Meyhoff. JAMA 2009; ;302:1543-50
Maneuvers to Increase Wound O$_2$

- Increase pO$_2$
- Combat vasoconstriction
  - Correct hypovolemia
  - Preserve normal core temperature
  - Control pain
  - Avoid vasoconstrictive drugs
Oxygenation Misconceptions

• Anemia is the culprit
• Hb saturation is informative
• Adequate arterial PO$_2$ for patient assures adequate $P_{sc}O_2$
• Transcutaneous PO$_2$ is informative
• Giving supplemental oxygen is enough
• Period of effect is 2-3 hours