

Do the Results of the OXYGEN Trial Change if Analyzed as “As-Treated”? A Secondary Analysis of the OXYGEN Trial

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INTRODUCTION:

The OXYGEN trial evaluated if elevated levels of perioperative oxygen reduce the risk of surgical site infections (SSI) after fixation of tibial pilon, tibial plateau, and calcaneus fractures. An “intention-to-treat” approach was used for the primary analysis, however, control group adherence to the assigned protocol was 83%. It is possible the study results may differ by re-analyzing using an “as treated” approach?

METHODS:

The original study randomized patients to receive 80% FiO₂ (treatment) or 30% FiO₂ (control) in the operating room and up to 2 hours in the recovery room. The primary outcome was a composite of either deep (treated with surgery) or superficial (treated with antibiotics alone) SSI within 182 days of definitive fixation. Secondary outcomes were deep and superficial surgical site infections within 90, 182, and 365 days of definitive fixation.

Adherence was defined using two different criteria. Criterion 1 required at least 80% of the surgery time less than or equal to 40% FiO₂ for the control group or greater than or equal to 70% FiO₂ for the treatment group. Criterion 2 required at least 80% of surgery time to fall within 20 – 40% (control) or 70 – 90% FiO₂ (treatment). Weighted Kaplan-Meier was used to estimate the probability of the primary and secondary outcomes as-treated.

RESULTS:

A total of 1231 patients ages 18 – 80 enrolled with tibial plateau, tibial pilon, or calcaneus fractures thought to be at elevated risk of infection.

Under Criterion 1, the primary outcome occurred in 7% (38/523) and 10% (49/471) of patients in the treatment and control groups, respectively (P=0.10). Deep infection occurred in 30 (6%) treatment and 30 (6.4%) control group patients (P=0.75). Superficial infection occurred in 9 (2%) treatment group patients and 20 (4%) control group patients (RR, 0.41; P=0.03).

Using Criterion 2, the primary outcome occurred in 7% (36/498) of treatment and 10% (48/468) of control patients (P=0.12). Deep infection occurred in 28 (5%) treatment and 29 (6%) control group patients (P=0.81). Superficial infection occurred in 9 (2%) treatment and 20 (4.3%) control group patients (RR=0.43; P=0.03).

DISCUSSION AND CONCLUSION:

When re-analyzing based on which patients actually received high or control levels of oxygen, the results are generally consistent with the original “intent to treat” analysis. Specifically, high perioperative oxygen still lowered the risk of superficial SSI but did not affect deep infections in tibial plateau, pilon, and calcaneus fractures. However, the composite outcome of any infection showed a similar trend but was no longer statistically significant. This might be due to the decreased precision of the smaller sample size or a selection bias of sicker patients requiring high oxygen in the control group. This analysis should reassure patients and clinicians that the findings of the trial appear to be robust to the analysis method.

