Supplementary Online Content


*eFigure 1.* Effect of Inhaled Nitric Oxide Gas vs Placebo on VAS Pain Score and Cumulative Morphine Equivalent

*eFigure 2.* Effect of Inhaled Nitric Oxide Gas vs Placebo on Nitrate and Nitrite

*eTable 1.* Cox Proportional Hazards Regression Analysis of VOC Resolution

*eTable 2.* Time to VOC Resolution, Cumulative Morphine Equivalents, and Baseline VAS Pain Score by Study Site

This supplementary material has been provided by the authors to give readers additional information about their work.
eFigure 1. Effect of Inhaled Nitric Oxide Gas Vs Placebo on VAS Pain Score and Cumulative Morphine Equivalent

A

Visual Analog Pain Score (cm), mean

Time, hours

Inhaled NO  Placebo

Error bars indicate 95% CI

B

Cumulative Morphine Equivalents (mg/kg), median

Time, hours

Inhaled NO  Placebo

Error bars indicate interquartile ranges
**eFigure 2.** Effect of Inhaled Nitric Oxide Gas vs Placebo on Nitrate and Nitrite

**A**

- **Graph A:**
  - Title: Plasma Nitrate (µmol/L), mean
  - X-axis: Time, days
  - Y-axis: Plasma Nitrate (µmol/L), mean
  - Legend: Inhaled NO, Placebo
  - Error bars indicate 95% CI

**B**

- **Graph B:**
  - Title: Plasma Nitrite (µmol/L), mean
  - X-axis: Time, days
  - Y-axis: Plasma Nitrite (µmol/L), mean
  - Legend: Inhaled NO, Placebo
  - Error bars indicate 95% CI
Whole Blood Nitrite (µmol/L), mean

Inhaled NO Placebo

Error bars indicate 95% CI
eTable 1. Cox Proportional Hazards Regression Analysis of VOC Resolution

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>RR (95% CI) (^1)</th>
<th>P Value (^2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Site</td>
<td>2.05 (1.4-3.0)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Gender</td>
<td>1.41 (0.9-2.1)</td>
<td>.098</td>
</tr>
<tr>
<td>Pain Score at Baseline</td>
<td>0.78 (0.7-0.9)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Alkaline Phosphatase</td>
<td>0.50 (0.3-0.8)</td>
<td>.002</td>
</tr>
<tr>
<td>Total Bilirubin</td>
<td>1.49 (1.1-2.0)</td>
<td>.004</td>
</tr>
</tbody>
</table>

\(^1\) RR of VOC resolution given for JHU and NIH relative to other sites, males relative to females, per unit increase in VAS, per unit increase of alkaline phosphatase, and per unit increase in total bilirubin, adjusted for all other variables in the model.

\(^2\) From Wald \(\chi^2\).
**eTable 2.** Time to VOC Resolution, Cumulative Morphine Equivalents, and Baseline VAS Pain Score by Study Site

<table>
<thead>
<tr>
<th>Study Site</th>
<th>Time to VOC Resolution, hours</th>
<th>Cumulative Morphine Equivalents, mg/kg</th>
<th>VAS Pain Score at Baseline, cm</th>
</tr>
</thead>
<tbody>
<tr>
<td>National Institutes of Health</td>
<td>64 39.7 (20.3-93.8)</td>
<td>63 1.9 (0.5-5.3)</td>
<td>64 7.1 (2.1)</td>
</tr>
<tr>
<td>Johns Hopkins University</td>
<td>14 53.6 (24.1-84.0)</td>
<td>14 1.5 (0.9-3.2)</td>
<td>14 6.6 (2.8)</td>
</tr>
<tr>
<td>Children’s Hospital Boston</td>
<td>6 75.9 (64.0-132.0)</td>
<td>6 3.1 (2.0-5.3)</td>
<td>6 5.6 (2.6)</td>
</tr>
<tr>
<td>Howard University</td>
<td>24 76.5 (46.0-176.1)</td>
<td>21 6.2 (2.6-11.8)</td>
<td>24 8.3 (1.4)</td>
</tr>
<tr>
<td>St. Christopher’s Hospital</td>
<td>14 87.8 (51.1-160.4)</td>
<td>14 4.9 (2.7-11.6)</td>
<td>14 8.0 (1.4)</td>
</tr>
<tr>
<td>Alta Bates Medical Center</td>
<td>8 93.5 (73.3-206.2)</td>
<td>7 12.4 (3.4-23.4)</td>
<td>8 8.3 (1.2)</td>
</tr>
<tr>
<td>Pooled Sites³</td>
<td>20 89.3 (53.4-106.3)</td>
<td>20 3.3 (1.5-5.1)</td>
<td>20 7.2 (2.1)</td>
</tr>
</tbody>
</table>

P Value² .002 .001 .02

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¹ University of Colorado Health Science Center, Brigham and Women’s Hospital, Case Western University, University of Alabama at Birmingham and Children’s Hospital of Pittsburgh.
² From Kruskal-Wallis test for differences in median time to resolution and total morphine equivalents; from ANOVA test for differences in mean VAS pain scores.