**Trial of Antibiotic Restraint in Presumed Pneumonia: A Surgical Infection Society Multicenter Pilot**

**Supplemental Appendix**

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**Supplemental Table A:**

**Demographics and Comorbidities: Site A**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Immediate** | **Specimen-Initiated** |  |
| Variable | 11 | 18 | p-value |
| Age (years) | 62 | (36-73) | 61 | (28-71) | 0.55 |
| Female sex | 4 | 36.4% | 4 | 22.2% | 0.43 |
| Race\* |  |  |  |  | 0.83 |
| White | 7 | 63.6% | 12 | 66.7% |  |
| Black | 3 | 27.3% | 2 | 11.1% |  |
| Other | 1 | 9.1% | 2 | 11.1% |  |
| Unknown | 0 | 0.0% | 2 | 11.1% |  |
| Ethnicity\* |  |  |  |  | -- |
| Hispanic or Latino | 0 | 0.0% | 0 | 0.0% |  |
| Non-Hispanic / Non-Latino | 11 | 100.0% | 16 | 88.9% |  |
| Unknown | 0 | 0.0% | 2 | 11.1% |  |
| Body Mass Index (BMI) | 32.2 | (25.7-36.4) | 28 | (23.3-34.8) | 0.28 |
| Comorbidities |  |  |  |  |  |
| Cardiac Disease | 3 | 27.3% | 3 | 16.7% | 0.65 |
| Renal Disease | 0 | 0.0% | 0 | 0.0% | -- |
| Hemodialysis | 1 | 9.1% | 0 | 0.0% | 0.38 |
| Inflammatory Bowel Disease | 0 | 0.0% | 0 | 0.0% | -- |
| Liver Disease | 0 | 0.0% | 2 | 11.1% | 0.51 |
| Malignancy | 1 | 9.1% | 0 | 0.0% | 0.38 |
| Peripheral Vascular Disease | 0 | 0.0% | 0 | 0.0% | -- |
| Pulmonary Disease | 0 | 0.0% | 4 | 22.2% | 0.27 |
| Other | 7 | 63.6% | 7 | 38.9% | 0.2 |
| Transfusion During Admission | 2 | 18.2% | 6 | 33.3% | 0.67 |
| ICU Admission Diagnosis |  | 0.0% |  | 0.0% |  |
| Trauma: Blunt | 7 | 63.6% | 14 | 77.8% | 0.43 |
| Trauma: Penetrating | 2 | 18.2% | 1 | 5.6% | 0.54 |
| EGS: Intra-Abdominal Infection | 0 | 0.0% | 1 | 5.6% | 1 |
| EGS: Non-IAI | 1 | 9.1% | 1 | 5.6% | 1 |
| Vascular | 0 | 0.0% | 1 | 5.6% | 1 |
| Scheduled Post-Surgical Admit | 0 | 0.0% | 0 | 0.0% | -- |
| Decompensation on Ward | 1 | 9.1% | 0 | 0.0% | 0.38 |
| Other | 0 | 0.0% | 0 | 0.0% | -- |
| Operation during Admission | 4 | 36.4% | 5 | 27.8% | 0.69 |
| Active infection on Admission | 0 | 0.0% | 1 | 5.6% | 1 |
| COVID-19 during Admission | 1 | 9.1% | 2 | 11.1% | 1 |
| Admission Scores |  |  |  |  |  |
| APACHE II | 13 | (8-22) | 12.5 | (7-15) | 0.66 |
| SOFA | 6 | (0-9) | 4 | (3-7) | 0.77 |
| Injury Severity Score\*\* | 22 | (19-25) | 25 | (16-34) | 0.72 |
| Glascow Coma Scale | 8 | (7-15) | 10 | (7-14) | 0.6 |
| qSOFA |  |  |  |  | 0.31 |
| 0 | 2 | 18.2% | 1 | 5.6% |  |
| 1 | 4 | 36.4% | 12 | 66.7% |  |
| 2 | 3 | 27.3% | 4 | 22.2% |  |
| 3 | 2 | 18.2% | 1 | 5.6% |  |

Data are presented as N/% or Median/IQR

\*p-values are calculated exclusive of patients with ‘unknown’ race or ethnicity

\*\*For trauma patients only

APACHE II = Acute Physiology and Chronic Health Evaluation II

SOFA = Sequential Organ Failure Assessment

qSOFA = Quick Sequential Organ Failure Assessment

**Supplemental Table B:**

**Demographics and Comorbidities: Site B**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Immediate** | **Specimen-Initiated** |  |
| Variable | 18 | 15 | p-value |
| Age (years) | 38.5 | (27.0-74.0) | 56 | (34-68) | 0.24 |
| Female sex | 5 | 27.8% | 5 | 33.3% | 0.73 |
| Race\* |  |  |  |  | 0.78 |
| White | 16 | 88.9% | 13 | 86.7% |  |
| Black | 1 | 5.6% | 2 | 13.3% |  |
| Other | 1 | 5.6% | 0 | 0.0% |  |
| Unknown | 0 | 0.0% | 0 | 0.0% |  |
| Ethnicity\* |  |  |  |  | 1 |
| Hispanic or Latino | 1 | 5.6% | 1 | 6.7% |  |
| Non-Hispanic / Non-Latino | 17 | 94.4% | 14 | 93.3% |  |
| Unknown | 0 | 0.0% | 0 | 0.0% |  |
| Body Mass Index (BMI) | 29.4 | (23.4-31.9) | 29.3 | (23.2-34.4) | 0.96 |
| Comorbidities |  |  |  |  |  |
| Cardiac Disease | 3 | 16.7% | 4 | 26.7% | 0.67 |
| Renal Disease | 1 | 5.6% | 1 | 6.7% | 1 |
| Hemodialysis | 0 | 0.0% | 0 | 0.0% | -- |
| Inflammatory Bowel Disease | 0 | 0.0% | 1 | 6.7% | 0.45 |
| Liver Disease | 0 | 0.0% | 0 | 0.0% | -- |
| Malignancy | 1 | 5.6% | 0 | 0.0% | 1 |
| Peripheral Vascular Disease | 0 | 0.0% | 2 | 13.3% | 0.2 |
| Pulmonary Disease | 1 | 5.6% | 4 | 26.7% | 0.15 |
| Other | 0 | 0.0% | 1 | 6.7% | 0.45 |
| Transfusion During Admission | 15 | 83.3% | 13 | 86.7% | 1 |
| ICU Admission Diagnosis |  |  |  |  |  |
| Trauma: Blunt | 16 | 88.9% | 13 | 86.7% | 1 |
| Trauma: Penetrating | 1 | 5.6% | 1 | 6.7% | 1 |
| EGS: Intra-Abdominal Infection | 0 | 0.0% | 0 | 0.0% | -- |
| EGS: Non-IAI | 0 | 0.0% | 1 | 6.7% | 0.45 |
| Vascular | 0 | 0.0% | 0 | 0.0% | -- |
| Scheduled Post-Surgical Admit | 1 | 5.6% | 0 | 0.0% | 1 |
| Decompensation on Ward | 0 | 0.0% | 0 | 0.0% | -- |
| Other | 0 | 0.0% | 0 | 0.0% | -- |
| Operation during Admission | 8 | 44.4% | 3 | 20.0% | 0.27 |
| Active infection on Admission | 1 | 5.6% | 1 | 6.7% | 1 |
| COVID-19 during Admission | 2 | 11.1% | 0 | 0.0% | 0.49 |
| Admission Scores |  |  |  |  |  |
| APACHE II | 18 | (13-25) | 20 | (15-26) | 0.67 |
| SOFA | 7 | (5-9) | 6 | (4-9) | 0.35 |
| Injury Severity Score\*\* | 27 | (24-33) | 26 | (21-38) | 0.92 |
| Glascow Coma Scale | 13 | (10-14) | 14 | (5-15) | 0.9 |
| qSOFA |  |  |  |  | 0.76 |
| 0 | 1 | 5.6% | 1 | 6.7% |  |
| 1 | 2 | 11.1% | 2 | 13.3% |  |
| 2 | 8 | 44.4% | 9 | 60.0% |  |
| 3 | 7 | 38.9% | 3 | 20.0% |  |

Data are presented as N/% or Median/IQR

\*p-values are calculated exclusive of patients with ‘unknown’ race or ethnicity

\*\*For trauma patients only

APACHE II = Acute Physiology and Chronic Health Evaluation II

SOFA = Sequential Organ Failure Assessment

qSOFA = Quick Sequential Organ Failure Assessment

**Supplemental Table C:**

**Demographics and Comorbidities: Site C**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Immediate** | **Specimen-Initiated** |  |
| Variable | 30 | 21 | p-value |
| Age (years) | 51.5 | (35-62) | 60 | (40-64) | 0.58 |
| Female sex | 6 | 20.0% | 2 | 9.5% | 0.45 |
| Race\* |  |  |  |  | 0.24 |
| White | 19 | 63.3% | 14 | 66.7% |  |
| Black | 7 | 23.3% | 7 | 33.3% |  |
| Other | 4 | 13.3% | 0 | 0.0% |  |
| Unknown | 0 | 0.0% | 0 | 0.0% |  |
| Ethnicity\* |  |  |  |  | 0.07 |
| Hispanic or Latino | 5 | 16.7% | 0 | 0.0% |  |
| Non-Hispanic / Non-Latino | 25 | 83.3% | 21 | 100.0% |  |
| Unknown | 0 | 0.0% | 0 | 0.0% |  |
| Body Mass Index (BMI) | 30 | (23.8-35.6) | 30.2 | (24.2-35.4) | 0.8 |
| Comorbidities |  |  |  |  |  |
| Cardiac Disease | 5 | 16.7% | 4 | 13.3% | 1 |
| Renal Disease | 0 | 0.0% | 0 | 0.0% | -- |
| Hemodialysis | 1 | 3.3% | 1 | 3.3% | 1 |
| Inflammatory Bowel Disease | 0 | 0.0% | 0 | 0.0% | -- |
| Liver Disease | 0 | 0.0% | 0 | 0.0% | -- |
| Malignancy | 1 | 3.3% | 0 | 0.0% | 1 |
| Peripheral Vascular Disease | 1 | 3.3% | 1 | 3.3% | 1 |
| Pulmonary Disease | 2 | 6.7% | 1 | 3.3% | 1 |
| Other | 2 | 6.7% | 3 | 10.0% | 0.64 |
| Transfusion During Admission | 23 | 76.7% | 7 | 23.3% | 0.002 |
| ICU Admission Diagnosis |  |  |  |  |  |
| Trauma: Blunt | 27 | 90.0% | 17 | 56.7% | 0.43 |
| Trauma: Penetrating | 1 | 3.3% | 3 | 10.0% | 0.29 |
| EGS: Intra-Abdominal Infection | 1 | 3.3% | 0 | 0.0% | 1 |
| EGS: Non-IAI | 0 | 0.0% | 1 | 3.3% | 0.23 |
| Vascular | 0 | 0.0% | 0 | 0.0% | -- |
| Scheduled Post-Surgical Admit | 0 | 0.0% | 0 | 0.0% | -- |
| Decompensation on Ward | 0 | 0.0% | 0 | 0.0% | -- |
| Other | 1 | 3.3% | 0 | 0.0% | -- |
| Operation during Admission | 13 | 43.3% | 7 | 23.3% | 0.47 |
| Active infection on Admission | 2 | 6.7% | 2 | 6.7% | 1 |
| COVID-19 during Admission | 0 | 0.0% | 0 | 0.0% | -- |
| Admission Scores |  |  |  |  |  |
| APACHE II | 15 | (13-18) | 17 | (7-19) | 1 |
| SOFA | 5 | (3-6) | 6 | (5-8) | 0.22 |
| Injury Severity Score\*\* | 21.5 | (11.0-35.5) | 17 | (11.5-35.0) | 0.75 |
| Glascow Coma Scale | 7 | (3-10) | 7 | (3-11) | 0.78 |
| qSOFA |  |  |  |  | 0.35 |
| 0 | 3 | 10.0% | 6 | 28.6% |  |
| 1 | 15 | 50.0% | 7 | 33.3% |  |
| 2 | 10 | 33.3% | 7 | 33.3% |  |
| 3 | 2 | 6.7% | 1 | 4.8% |  |

Data are presented as N/% or Median/IQR

\*p-values are calculated exclusive of patients with ‘unknown’ race or ethnicity

\*\*For trauma patients only

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SOFA = Sequential Organ Failure Assessment

qSOFA = Quick Sequential Organ Failure Assessment

**Supplemental Table D:**

**Demographics and Comorbidities: Site D**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Immediate** | **Specimen-Initiated** |  |
| Variable | 34 | 39 | p-value |
| Age (years) | 36.5 | (24.0-52.0) | 51 | (36-64) | 0.04 |
| Female sex | 5 | 14.7% | 8 | 20.5% | 0.52 |
| Race\* |  |  |  |  | 0.56 |
| White | 27 | 79.4% | 28 | 71.8% |  |
| Black | 3 | 8.8% | 7 | 17.9% |  |
| Other | 3 | 8.8% | 4 | 10.3% |  |
| Unknown | 1 | 2.9% | 0 | 0.0% |  |
| Ethnicity\* |  |  |  |  | 1 |
| Hispanic or Latino | 3 | 8.8% | 4 | 10.3% |  |
| Non-Hispanic / Non-Latino | 31 | 91.2% | 35 | 89.7% |  |
| Unknown | 0 | 0.0% | 0 | 0.0% |  |
| Body Mass Index (BMI) | 30 | (24.4-33.5) | 27.7 | (24.7-32.6) | 0.96 |
| Comorbidities |  |  |  |  |  |
| Cardiac Disease | 3 | 8.8% | 12 | 30.8% | 0.02 |
| Renal Disease | 0 | 0.0% | 0 | 0.0% | -- |
| Hemodialysis | 0 | 0.0% | 0 | 0.0% | -- |
| Inflammatory Bowel Disease | 0 | 0.0% | 0 | 0.0% | -- |
| Liver Disease | 0 | 0.0% | 1 | 2.6% | 1 |
| Malignancy | 0 | 0.0% | 1 | 2.6% | 1 |
| Peripheral Vascular Disease | 0 | 0.0% | 1 | 2.6% | 1 |
| Pulmonary Disease | 1 | 2.9% | 3 | 7.7% | 0.62 |
| Other | 3 | 8.8% | 11 | 28.2% | 0.04 |
| Transfusion During Admission | 23 | 67.6% | 29 | 74.4% | 0.53 |
| ICU Admission Diagnosis |  |  |  |  |  |
| Trauma: Blunt | 29 | 85.3% | 34 | 87.2% | 0.82 |
| Trauma: Penetrating | 5 | 14.7% | 5 | 12.8% | 0.82 |
| EGS: Intra-Abdominal Infection | 0 | 0.0% | 0 | 0.0% | -- |
| EGS: Non-IAI | 0 | 0.0% | 0 | 0.0% | -- |
| Vascular | 0 | 0.0% | 0 | 0.0% | -- |
| Scheduled Post-Surgical Admit | 0 | 0.0% | 0 | 0.0% | -- |
| Decompensation on Ward | 0 | 0.0% | 0 | 0.0% | -- |
| Other | 0 | 0.0% | 0 | 0.0% | -- |
| Operation during Admission | 10 | 29.4% | 5 | 12.8% | 0.08 |
| Active infection on Admission | 0 | 0.0% | 1 | 2.6% | 1 |
| COVID-19 during Admission | 2 | 5.9% | 1 | 2.6% | 0.59 |
| Admission Scores |  |  |  |  |  |
| APACHE II | 14.5 | (11.0-19.0) | 16 | (12.0-20.0) | 0.56 |
| SOFA | 6 | (4-7) | 6 | (4-7) | 0.87 |
| Injury Severity Score\*\* | 27.5 | (16.0-38.0) | 25 | (18.0-30.0) | 0.76 |
| Glascow Coma Scale | 7 | (3-11) | 6 | (3-11) | 0.49 |
| qSOFA |  |  |  |  | 0.96 |
| 0 | 0 | 0.0% | 1 | 2.6% |  |
| 1 | 18 | 52.9% | 21 | 53.8% |  |
| 2 | 15 | 44.1% | 15 | 38.5% |  |
| 3 | 1 | 2.9% | 2 | 5.1% |  |

Data are presented as N/% or Median/IQR

\*p-values are calculated exclusive of patients with ‘unknown’ race or ethnicity

\*\*For trauma patients only

APACHE II = Acute Physiology and Chronic Health Evaluation II

SOFA = Sequential Organ Failure Assessment

qSOFA = Quick Sequential Organ Failure Assessment

**Table E:**

**Overall Outcomes: Per-Protocol**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Immediate** | **Specimen-Initiated** |  |
| **Variable** | 69 | 77 | **p-value** |
| Hours from Culture to Antibiotics | 1 | (0-2) | 8.5 | (0-27) | <0.0001 |
| Adherence | 69 | 100.0% | 77 | 100.0% | -- |
| Ventilator-Free Alive Days at 30 Days | 9 | (0-17) | 7 | (0-16) | 0.96 |
| Mortality due to pneumonia | 1 | 1.4% | 1 | 1.3% | 1 |
| ICU Mortality | 10 | 14.5% | 13 | 16.9% | 0.69 |
| All-cause 30-day Mortality | 12 | 17.4% | 15 | 19.5% | 0.75 |

**Table F:**

**Vasopressors within 24 hours of Antibiotics**

|  |  |  |  |
| --- | --- | --- | --- |
| Intention-to-treat | **Immediate** | **Specimen-Initiated** |  |
| **Variable** | 34 | 30 | **p-value** |
| Hours from Culture to Antibiotics\* | 0 | (0-1) | 1 | (0-21) | 0.08 |
| Adherence | 24 | 70.6% | 23 | 76.7% | 0.58 |
| Ventilator-Free Alive Days at 30 Days | 0 | (0-12) | 1 | (0-15) | 0.93 |
| Mortality due to pneumonia | 0 | 0.0% | 1 | 3.3% | 0.47 |
| ICU Mortality | 7 | 20.6% | 9 | 30.0% | 0.39 |
| All-cause 30-day Mortality | 8 | 23.5% | 10 | 33.3% | 0.38 |
|  |  |  |  |  |  |
| Per-Protocol | **Immediate** | **Specimen-Initiated** |  |
| **Variable** | 24 | 23 | **p-value** |
| Hours from Culture to Antibiotics\* | 0.38 | (0-1.5) | 1 | (1-21) | 0.35 |
| Adherence | 24 | 100% | 23 | 100% | -- |
| Ventilator-Free Alive Days at 30 Days | 0 | (0-10) | 0 | (0-8) | 0.77 |
| Mortality due to pneumonia | 0 | 0.0% | 1 | 4.3% | 0.49 |
| ICU Mortality | 5 | 20.8% | 8 | 34.8% | 0.29 |
| All-cause 30-day Mortality | 6 | 25.0% | 8 | 34.8% | 0.46 |

Patients may progress to requiring vasopressors at a timepoint after the culture is obtained.

**Table G:**

**Increase in SOFA of ≥2 from Admission to Culture**

|  |  |  |  |
| --- | --- | --- | --- |
| Intention-to-treat | **Immediate** | **Specimen-Initiated** |  |
| **Variable** | 40 | 42 | **p-value** |
| Hours from Culture to Antibiotics | 0.13 | (0-1) | 15 | (0-27.5) | 0.002 |
| Adherence | 30 | 75.0% | 34 | 81.0% | 0.52 |
| Ventilator-Free Alive Days at 30 Days | 6 | (0-14) | 4.5 | (0-13) | 0.75 |
| Mortality due to pneumonia | 1 | 2.5% | 1 | 2.4% | 1 |
| ICU Mortality | 9 | 22.5% | 10 | 23.8% | 0.89 |
| All-cause 30-day Mortality | 10 | 25.0% | 12 | 28.6% | 0.72 |
|  |  |  |  |  |  |
| Per-Protocol | **Immediate** | **Specimen-Initiated** |  |
| **Variable** | 30 | 34 | **p-value** |
| Hours from Culture to Antibiotics | 0.5 | (0-1) | 11 | (0-24) | 0.01 |
| Adherence | 30 | 100% | 34 | 100% | -- |
| Ventilator-Free Alive Days at 30 Days | 4.5 | (0-15) | 3.5 | (0-13) | 1 |
| Mortality due to pneumonia | 1 | 3.3% | 1 | 2.9% | 1 |
| ICU Mortality | 7 | 23.3% | 10 | 29.4% | 0.58 |
| All-cause 30-day Mortality | 8 | 26.7% | 11 | 32.4% | 0.62 |

**Table H:**

**Patients with Pneumonia**

|  |  |  |  |
| --- | --- | --- | --- |
| Intention-to-treat | **Immediate** | **Specimen-Initiated** |  |
| **Variable** | 66 | 56 | **p-value** |
| Hours from Culture to Antibiotics | 0.25 | (0-2) | 12 | (1-28) | <0.0001 |
| Adherence | 55 | 83.3% | 47 | 83.9% | 0.93 |
| Ventilator-Free Alive Days at 30 Days | 6.5 | (0-15) | 7.5 | (0-19) | 0.51 |
| Mortality due to pneumonia | 1 | 1.5% | 0 | 0.0% | 1 |
| ICU Mortality | 11 | 16.7% | 5 | 8.9% | 0.28 |
| All-cause 30-day Mortality | 12 | 18.2% | 6 | 10.7% | 0.25 |
|  |  |  |  |  |  |
| Per-Protocol | **Immediate** | **Specimen-Initiated** |  |
| **Variable** | 55 | 47 | **p-value** |
| Hours from Culture to Antibiotics | 1 | (0-2) | 12 | (2-30) | <0.001 |
| Adherence | 55 | 100% | 47 | 100% | -- |
| Ventilator-Free Alive Days at 30 Days | 8 | (0-15) | 7 | (0-17) | 0.81 |
| Mortality due to pneumonia | 1 | 1.8% | 0 | 0.0% | 1 |
| ICU Mortality | 9 | 16.4% | 5 | 10.6% | 0.4 |
| All-cause 30-day Mortality | 10 | 18.2% | 6 | 12.8% | 0.45 |

**Table I:**

**Excluding Patients on Antibiotics for Another Indication**

|  |  |  |  |
| --- | --- | --- | --- |
| Intention-to-treat | **Immediate** | **Specimen-Initiated** |  |
| **Variable** | 83 | 76 | **p-value** |
| Hours from Culture to Antibiotics | 0 | (0-2) | 12 | (1-28) | <0.0001 |
| Adherence | 61 | 73.5% | 60 | 78.9% | 0.42 |
| Ventilator-Free Alive Days at 30 Days | 9 | (0-17) | 7 | (0-18) | 0.96 |
| Mortality due to pneumonia | 2 | 2.4% | 1 | 1.3% | 1 |
| ICU Mortality | 13 | 15.7% | 11 | 14.5% | 0.83 |
| All-cause 30-day Mortality | 15 | 18.1% | 13 | 17.1% | 0.87 |
|  |  |  |  |  |  |
| Per-Protocol | **Immediate** | **Specimen-Initiated** |  |
| **Variable** | 61 | 60 | **p-value** |
| Hours from Culture to Antibiotics | 1 | (0-2) | 11.3 | (1.5-30) | <0.0001 |
| Adherence | 61 | 100% | 60 | 100% | -- |
| Ventilator-Free Alive Days at 30 Days | 10 | (0-17) | 6.5 | (0-16.5) | 0.57 |
| Mortality due to pneumonia | 1 | 1.6% | 1 | 1.7% | 1 |
| ICU Mortality | 8 | 13.1% | 10 | 16.7% | 0.58 |
| All-cause 30-day Mortality | 10 | 16.4% | 11 | 18.3% | 0.78 |