**Supplementary Material**

**Prevalence, Risk Factors, and Outcomes Associated with Delayed Second Doses of Antibiotics in Sepsis at a Large Academic Medical Center**

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**Table of Contents**

**Supplementary Table 1: Best Practice Alert (BPA) Criteria**……………………………….....3

**Supplementary Table 2. Antipseudomonal Beta-lactam Dosing**……………………………...4

**Supplementary Table 3. Vancomycin Dosing**………………………………………………….6

**Supplementary Table 4. Fluid Administration**...........................................................................7

**Supplementary Table 5. Subgroup Analysis: Patients Admitted to Non-Intensive Care Units**................................................................................................................................................8

**Supplementary Table 6. Regression Analysis Evaluating the Association Between Delayed Second Doses of Antibiotics and In-hospital Mortality in Patients Admitted to Non-Intensive Care Units**......................................................................................................................9

**Supplementary Figure 1. Vancomycin Dosing in Renal Insufficiency**...................................10

**Supplementary Table 1. Best Practice Alert (BPA) Criteria**

|  |  |
| --- | --- |
| **BPA** | **Criteria** |
| Sepsis | Possible*a* or high suspicion*b* of infection and ≥ 1 of the following:* Systolic blood pressure < 90 mm Hg
* Lactate > 2.0 mmol/L
* Creatinine > 2.0 mg/dL (acute rise)
* Initiation of mechanical or non-invasive positive pressure ventilation
 |
| Septic shock | Possible*a* or high suspicion*b* of infection and ≥ 1 of the following: * Systolic blood pressure < 90 mm Hg that persists for > 3 hours
* Lactate ≥ 4 mmol/L
 |

*a*Possible infection: Temperature > 100.4°F, white blood cell (WBC) count > 15 x 109/L, urinalysis with > 20 WBC, culture ordered, emergency department (ED) screen positive for “possible infection”

*b*High suspicion of infection: Intravenous antibiotics, bands ≥ 5%, ED screen positive for “looks sick”

**Supplementary Table 2. Antipseudomonal Beta-Lactam Dosing**

|  |  |  |
| --- | --- | --- |
| **Antibiotic** | **Creatinine clearance (mL/min)** | **Recommended dosing interval** |
| Aztreonam | >50 | Q8H |
| 10-50 |
| <10 |
| Hemodialysis |
| Cefepime | ≥60 | Q8H |
| 30-59 | Q12H |
| 10-29 | Q24H |
| <10 |
| Hemodialysis | 1 g Q24H or 2 g post-HD |
| Ceftazidime | >50 | Q8H |
| 31-50 | Q12H |
| 16-30 | Q24H |
| 5-15 |
| <5 | Q48H |
| Hemodialysis | 1 g Q24H or 2 g post-HD |
| Imipenem-cilastatin | ≥60 | Q6H |
| 30-59 | Q8H |
| 15-29 | Q12H |
| Hemodialysis |
| Meropenem | >50 | Q8H |
| 26-50 | Q12H |
| 10-25 |
| <10 | Q24H |
| Hemodialysis |
| Piperacillin-tazobactam | >40 | Q6H |
| 20-40 |
| <20 |
| Hemodialysis | Q8H |

**Supplementary Table 3. Vancomycin Dosing**

|  |  |  |  |
| --- | --- | --- | --- |
| **Age (years)** | 18-49 | 50-79 | ≥80 |
| **Creatinine clearance (mL/min)** | ≥90 | 50-89 | ≤49 | ≥50 | ≤49 | ≥60 | ≤59 |
| **Recommended interval** | Q8H | Q12H | Q24H | Q12H | Q24H | Q12H | Q24H |

**Supplementary Table 4. Fluid Administration**

|  |  |  |  |
| --- | --- | --- | --- |
| **Variable** | **Delayed group** **(n=123)** | **Non-delayed group (n=326)** | ***p*** |
| Received 30 mL/kg of fluid within 3 hours of BPA*a* | 39 (31.7) | 115 (35.3) | 0.48 |
| Type of crystalloid administered*a* |  |  |  |
|  Normal saline | 100 (81.3) | 242 (74.2) | 0.12 |
|  Lactated Ringer’s  | 56 (45.5) | 161 (49.4) | 0.47 |
|  Dextrose 5% in water | 2 (1.6) | 4 (1.2) | 0.74 |
|  Other*b* | 11 (8.9) | 16 (4.9) | 0.11 |

BPA, best practice alert

*a*Data presented as n (%)

*b*Other fluids include dextrose 10% in water, ½ normal saline, combination fluids with dextrose and sodium chloride, sodium bicarbonate, and electrolyte containing fluids (e.g., normal saline with potassium chloride)

**Supplementary Table 5. Subgroup Analysis: Patients Admitted to Non-Intensive Care Units**

|  |  |  |  |
| --- | --- | --- | --- |
| **Outcome** | **Delayed group****(n=49)** | **Non-delayed group (n=122)** | ***p*** |
| In-hospital mortality*a* | 9 (18.4) | 7 (5.7) | 0.01 |
| Discharge to hospice*a* | 4 (8.2) | 7 (5.7) | 0.56 |
| Hospital length of stay (days)*b* | 5.0 [4.0-9.0] | 7.0 [4.0-11.0] | 0.08 |

*a*Data presented as n (%)

*b*Data presented as median [interquartile range]

**Supplementary Table 6. Regression Analysis Evaluating the Association Between Delayed Second Doses of Antibiotics and In-hospital Mortality in Patients Admitted to Non-Intensive Care Units**

|  |  |  |
| --- | --- | --- |
| **Variable** | **OR (95% CI)** | ***p*** |
| Delay in second dose | 4.10 (1.32-12.79) | 0.02 |
| Weight (per 1 point BMI increase) | 0.98 (0.95-1.02) | 0.31 |
| Malignancy | 1.92 (0.56-6.55) | 0.30 |
| Respiratory infection | 2.04 (0.63-6.62) | 0.23 |
| Non-ED location at time second dose due | 1.77 (0.16-20.01) | 0.65 |
| Time in ED (per hour) | 0.97 (0.82-1.15) | 0.72 |
| SOFA score (per 1 point increase) | 1.34 (1.08-1.66) | 0.01 |
| Initiation of stress dose steroids within 24 h of inclusion BPA | 1.66 (0.30-9.06) | 0.56 |

BMI, body mass index; ED, emergency department; SOFA, sequential organ failure assessment; BPA, best practice alert

**Supplementary Figure 1. Vancomycin Dosing in Renal Insufficiency**

****Abbreviations: HD, hemodialysis